

Revisiting lymph node guidelines: limited lymph node examination might be sufficient for elderly gastric cancer patients

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Background: Whether limited examined lymph node (ELN) number is comparable to recommended ELN number for long-term outcomes remains controversial in elderly gastric cancer (GC) patients. The purpose of this study was to assess the long-term survival between limited ELN number and recommended ELN number in elderly GC patients.

Methods: Elderly GC patients over 75 years old from the Surveillance, Epidemiology, and End Results (SEER) database were retrospectively reviewed. The long-term cancer-specific survival (CSS) and overall survival (OS) were compared between the limited ELN number group (ELN <15, limited group) and recommended ELN number (ELN ≥15, recommended group).

Results: In total, 1,521 elderly GC patients were divided into the limited group (793 patients, 52.1%) and recommended group (728 patients, 47.9%). The 1-, 3-, and 5-year CSS in the limited group and recommended group were 76.5% vs. 78.6%, 55.0% vs. 58.5%, 47.8% vs. 50.4%. The 1-, 3-, and 5-year OS in the limited group and recommended group were 70.7% vs. 74.8%, 45.1% vs. 50.7%, 33.7% vs. 39.4%. The Kaplan-Meier survival curve analysis of CSS demonstrated no statistical significance between the two groups (P=0.31). Moreover, the OS was similar between the two groups in the elderly GC patients who underwent total gastrectomy (P=0.16). However, the OS were significant shorter in the limited group in elderly GC patients who underwent proximal and distal gastrectomy (both P<0.001).

Conclusions: Limited ELN number might be sufficient for elderly GC patients with total gastrectomy. Prospective studies with a larger sample size are required to validated these results.

Keywords: Gastric cancer (GC); lymphadenectomy; elderly; survival

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Introduction

Gastric cancer (GC) has the fourth highest morbidity and mortality rate in the world (1). As a result of population aging, the proportion of elderly patients diagnosed with cancer is increasing. According to the data from the Surveillance, Epidemiology, and End Results (SEER) database, more than a third of GC patients were over 75 years old at diagnosis (2). The perioperative management of elderly GC patients remains

a challenge, because they are more likely suffering from chronic illnesses (3). Several studies have demonstrated that the risk of postoperative complications and mortality significantly increases in elderly GC patients underwent gastrectomy (4-6). In addition, evidence has shown that gastrectomy with adequate lymph node dissection might increase the incidence of intra-abdominal abscesses (7). Therefore, whether more than 15 lymph nodes resection must be performed in elderly GC patients has become a significant concern.

Currently, whether limited examined lymph node (ELN) number is comparable to recommended ELN number for long-term outcomes remains controversial in elderly GC patients. A retrospective multi-institutional demonstrated that D2 lymphadenectomy and limited lymphadenectomy are comparable in terms of cancer-specific survival (CSS) and recurrence-free survival (RFS) rates (7). While in a recent study conducted by Ko *et al.*, the results demonstrated that the 3-year RFS rate was higher in D2 lymphadenectomy group (8). However, there studies were limited by small sample size, yielding inconclusive results.

As such, the present study aimed to evaluate the long-term outcomes between limited ELN number and recommended ELN number in elderly GC patients based on the SEER database. We present this article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-24-1477/rc).

Methods

Patients

GC patients in the SEER database between 2000 to 2019 were retrospectively retrieved and reviewed through SEER*Stat Software (version 8.4.0.1). The SEER database is a publicly accessible database and therefore ethical review and informed consent are exempted. The main inclusion criteria were: (I) patients who were pathologically diagnosed as gastric adenocarcinoma; (II) patients were

Highlight box

Key findings

 Limited examined lymph node number might be sufficient for elderly gastric cancer (GC) patients with total gastrectomy.

What is known and what is new?

- Radical resection of GC requires the removal of at least 15 lymph nodes, which can increase surgical trauma. However, the risk of radical GC surgery is significantly higher in elderly patients.
- The present study evaluated the long-term outcomes between limited examined lymph node number and recommended examined lymph node number in elderly GC patients based on the Surveillance, Epidemiology, and End Results database.

What is the implication, and what should change now?

 More prospective clinical studies on lymph node dissection strategies for elderly patients with GC should be carried out. over 75 years old at diagnosis; (III) patients who underwent curative gastrectomy; (IV) patients who received lymph nodes resection; (V) patients who were diagnosed with first primary malignant GC. The main exclusion criteria were: (I) patients with unknown specific age; (II) patients with unknown race; (III) patients with unknown specific tumor location; (IV) patients with unknown gastrectomy type; (V) patients with unknown tumor stage; (VI) patients with unknown information about follow-up. Finally, 1,521 elderly GC patients were enrolled into the present study.

Clinicopathological parameters and outcomes

The clinicopathological variables included in the study were age, sex, race, tumor location, differentiation, tumor stage, gastrectomy type, tumor size, perioperative chemotherapy, and perioperative radiotherapy. According to the number of ELNs, the patients were divided into the limited ELN number group (ELN <15, limited group) and recommended ELN number (ELN ≥15, recommended group).

The main outcome in the current study was CSS time, which was defined as the time from diagnosis to the death attributed to GC. The second outcome was overall survival (OS) time, which was defined as the time from diagnosis to the death attributed to any reasons.

Statistical analysis

Data analysis in the study was conducted using SPSS 22 (IBM Corp, Armonk, NY, USA) and R software (R software, version 4.1.2). The continuous variables were described with median and interquartile range (IQR), while the categorical variables were expressed with frequencies and proportions. Comparisons between groups were performed with Chisquared test and Mann-Whitney U method. Univariate Cox regression analysis was used to screen potential prognostic factors, and then variables with P<0.1 in univariate Cox regression analysis were included in multivariate Cox regression analysis to identify independent prognostic factors. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) were used to present the survival analysis results. The survival curves were drawn using R package "survminer". A P value of <0.05 was regarded as statistically significant. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Results

Basic characteristics

In total, 1,521 elderly GC patients were divided into the limited group (793 patients, 52.1%) and recommended group (728 patients, 47.9%). The median age in the present study was 80 (IQR, 77–84) years. The recommended group tended to have higher proportion of T stage (P<0.001), lymph node metastasis (P<0.001), and preoperative chemotherapy (P=0.045). In terms of age (P=0.36), sex (P=0.89), race (P=0.07), months from diagnosis to treatment (P=0.31), differentiation (P=0.051), preoperative radiotherapy (P=0.94), and postoperative radiotherapy (P=0.09), there was no significant difference between the two groups. The demographic details of the patients were shown in *Table 1*.

Long-term survival analysis

The 1-, 3-, and 5-year CSS in the total elderly GC patients were 76.6%, 56.2%, and 49.0%, respectively. The 1-, 3-,

and 5-year CSS in the limited group and recommended group were 76.5% vs. 78.6%, 55.0% vs. 58.5%, 47.8% vs. 50.4%. The Kaplan-Meier survival curve analysis of CSS demonstrated no statistical significance between the two groups (P=0.31, Figure 1A). Multivariate Cox analysis illustrated that Asian or Pacific Islander, over one month from diagnosis to the treatment, tumor located at antrum/ pylorus were independent protective factors, while older age, undifferentiation (G4), advanced T stage, and advanced N stage were independent risk factors of CSS for elderly GC patients (Table 2).

The 1-, 3-, and 5-year OS in the total elderly GC patients were 72.7%, 47.8%, and 36.4%, respectively. The 1-, 3-, and 5-year OS in the limited group and recommended group were 70.7% vs. 74.8%, 45.1% vs. 50.7%, 33.7% vs. 39.4%. The recommended group had significantly longer OS than limited group (P=0.009, Figure 1B). In the multivariate Cox analysis, the recommended group also was the independent protective factor of OS (HR: 0.687, 95% CI: 0.606–0.779, P<0.001) for elderly GC patients (Table 3).

Table 1 The demographic characteristics of elderly gastric cancer patients

| Variables | Total (n=1,521) | ELN <15 (n=793) | ELN ≥15 (n=728) | P value | Method |
|---|-----------------|-----------------|-----------------|---------|------------------|
| Age, years, median [IQR] | 80 [77, 84] | 81 [77, 84] | 80 [77, 83] | 0.36 | Mann-Whitney U |
| Sex, n (%) | | | | 0.89 | Chi-squared test |
| Female | 810 (53.254) | 421 (53.090) | 389 (53.434) | | |
| Male | 711 (46.746) | 372 (46.910) | 339 (46.566) | | |
| Race, n (%) | | | | 0.07 | Chi-squared test |
| White | 969 (63.708) | 524 (66.078) | 445 (61.126) | | |
| Black | 158 (10.388) | 86 (10.845) | 72 (9.890) | | |
| Asian or Pacific Islander | 389 (25.575) | 181 (22.825) | 208 (28.571) | | |
| American Indian/Alaska Native | 5 (0.329) | 2 (0.252) | 3 (0.412) | | |
| Months from diagnosis to treatment, n (%) | | | | 0.31 | Chi-squared test |
| ≤1 month | 1,142 (75.082) | 604 (76.166) | 538 (73.901) | | |
| >1 month | 379 (24.918) | 189 (23.834) | 190 (26.099) | | |
| Location, n (%) | | | | <0.001 | Chi-squared test |
| Cardia/fundus | 370 (24.326) | 177 (22.320) | 193 (26.511) | | |
| Body | 176 (11.571) | 87 (10.971) | 89 (12.225) | | |
| Antrum/pylorus | 832 (54.701) | 470 (59.269) | 362 (49.725) | | |
| Total stomach | 143 (9.402) | 59 (7.440) | 84 (11.538) | | |

Table 1 (continued)

Table 1 (continued)

| Variables | Total (n=1,521) | ELN <15 (n=793) | ELN ≥15 (n=728) | P value | Method |
|-----------------------------------|-----------------|-----------------|-----------------|---------|------------------|
| Tumor size, n (%) | | | | <0.001 | Chi-squared test |
| <5 cm | 893 (58.711) | 506 (63.808) | 387 (53.159) | | |
| ≥5 cm | 628 (41.289) | 287 (36.192) | 341 (46.841) | | |
| Gastrectomy, n (%) | | | | <0.001 | Chi-squared test |
| Distal | 832 (54.701) | 478 (60.277) | 354 (48.626) | | |
| Proximal | 421 (27.679) | 217 (27.364) | 204 (28.022) | | |
| Total | 268 (17.620) | 98 (12.358) | 170 (23.352) | | |
| Differentiation, n (%) | | | | 0.051 | Chi-squared test |
| G1 | 97 (6.377) | 60 (7.566) | 37 (5.082) | | |
| G2 | 500 (32.873) | 275 (34.678) | 225 (30.907) | | |
| G3 | 895 (58.843) | 444 (55.990) | 451 (61.951) | | |
| G4 | 29 (1.907) | 14 (1.765) | 15 (2.060) | | |
| T stage, n (%) | | | | <0.001 | Chi-squared test |
| 1 | 416 (27.350) | 237 (29.887) | 179 (24.588) | | |
| 2 | 478 (31.427) | 276 (34.805) | 202 (27.747) | | |
| 3 | 425 (27.942) | 187 (23.581) | 238 (32.692) | | |
| 4 | 202 (13.281) | 93 (11.728) | 109 (14.973) | | |
| N stage, n (%) | | | | <0.001 | Chi-squared test |
| 0 | 712 (46.811) | 425 (53.594) | 287 (39.423) | | |
| 1 | 365 (23.997) | 217 (27.364) | 148 (20.330) | | |
| 2 | 204 (13.412) | 96 (12.106) | 108 (14.835) | | |
| 3 | 240 (15.779) | 55 (6.936) | 185 (25.412) | | |
| Preoperative radiotherapy, n (%) | | | | 0.94 | Chi-squared test |
| No | 1,461 (96.055) | 762 (96.091) | 699 (96.016) | | |
| Yes | 60 (3.945) | 31 (3.909) | 29 (3.984) | | |
| Preoperative chemotherapy, n (%) | | | | 0.045 | Chi-squared test |
| No | 1,399 (91.979) | 740 (93.317) | 659 (90.522) | | |
| Yes | 122 (8.021) | 53 (6.683) | 69 (9.478) | | |
| Postoperative chemotherapy, n (%) | | | | <0.001 | Chi-squared test |
| No | 1,137 (74.753) | 627 (79.067) | 510 (70.055) | | |
| Yes | 384 (25.247) | 166 (20.933) | 218 (29.945) | | |
| Postoperative radiotherapy, n (%) | | | | 0.09 | Chi-squared test |
| No | 1,321 (86.851) | 700 (88.272) | 621 (85.302) | | |
| Yes | 200 (13.149) | 93 (11.728) | 107 (14.698) | | |

IQR, interquartile range; ELN, examined lymph node.

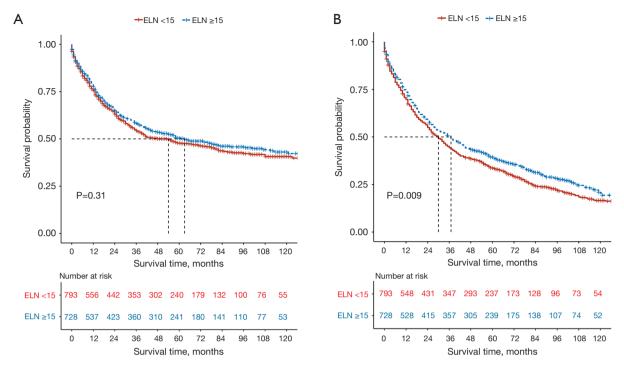


Figure 1 The Kaplan-Meier survival curve analysis between the limited lymphadenectomy group and D2 lymphadenectomy group. (A) Cancer-specific survival; (B) overall survival. ELN, examined lymph node.

Stratified analysis

Considering the impact of gastrectomy type on the number of lymph nodes dissected, we compared the survival difference between the two groups according to different gastrectomy type. The results demonstrated that the CSS were similar between limited group and recommended group in the elderly GC patients, despite the extent of gastric resection (Figure 2A-2C). However, the Kaplan-Meier survival curve analysis (Figure 2D) and multivariate Cox analysis demonstrated that the OS were significant shorter in the limited group in elderly GC patients who underwent proximal gastrectomy (P<0.001) (Table S1). In addition, the OS was similar between the two groups in the elderly GC patients who underwent distal gastrectomy and total gastrectomy (Figure 2E,2F). Moreover, multivariate Cox analysis also demonstrated that the OS was significant shorter in the limited group in elderly GC patients who underwent distal gastrectomy (Table S2).

Furthermore, we stratified elderly GC patients according to the basic clinicopathologic characteristics and compared the CSS between limited group and recommended group. The D2 lymphadenectomy showed CSS benefit in the subgroups of tumor size ≥ 5 cm (P=0.04), N0 stage

(P=0.01), N1 stage (P<0.001), T3 stage (P=0.01), and poor differentiation (G3) (P=0.04). The results were illustrated in the Figure~3.

Discussion

Evidence has shown that for GC patients who underwent adequate lymphadenectomy, the elderly group are more likely to have postoperative complications and higher mortality rates (9). However, whether limited lymphadenectomy could achieve comparable outcomes in elderly GC patients compared with D2 lymphadenectomy remains a matter of debate. The present study provided the positive evidence for the limited ELN number in the elderly GC patients. We demonstrated that the CSS were similar between limited group and recommended group in elderly GC patients regardless of the gastrectomy type.

Currently, D2 lymphadenectomy is an important part of standard surgical treatment for GC. However, careful lymph node dissection might prolong the operation time and increase the amount of intraoperative blood loss for elderly GC patients (7,8). Several studies have demonstrated that limited lymphadenectomy does not reduce the survival

Table 2 The univariate and multivariate Cox analysis of cancer-specific survival in elderly gastric cancer patients

| Variables – | Univariate analysis | | | Multivariate analysis | | | |
|------------------------------------|---------------------|-------------|---------|-----------------------|-------------|---------|--|
| variables | HR | 95% CI | P value | HR | 95% CI | P value | |
| Age | 1.023 | 1.007-1.039 | 0.005 | 1.033 | 1.017-1.050 | < 0.001 | |
| Sex | | | | | | | |
| Female | | Reference | | | | | |
| Male | 0.911 | 0.789-1.052 | 0.20 | | | | |
| Race | | | | | | | |
| White | | Reference | | | Reference | | |
| Black | 1.071 | 0.849-1.351 | 0.56 | 1.018 | 0.802-1.294 | 0.88 | |
| Asian or Pacific Islander | 0.756 | 0.635-0.900 | 0.002 | 0.723 | 0.605-0.886 | < 0.001 | |
| American Indian/Alaska Native | 1.587 | 0.510-4.938 | 0.43 | 1.228 | 0.385-3.918 | 0.73 | |
| Months from diagnosis to treatment | | | | | | | |
| ≤1 month | | Reference | | | Reference | | |
| >1 month | 0.616 | 0.515-0.737 | < 0.001 | 0.676 | 0.562-0.814 | < 0.001 | |
| _ocation | | | | | | | |
| Cardia/fundus | | Reference | | | Reference | | |
| Body | 0.967 | 0.753-1.243 | 0.79 | 0.869 | 0.663-1.139 | 0.31 | |
| Antrum/pylorus | 0.854 | 0.719-1.014 | 0.07 | 0.623 | 0.493-0.787 | <0.001 | |
| Total stomach | 1.239 | 0.956-1.605 | 0.11 | 0.751 | 0.565-0.999 | 0.049 | |
| Tumor size | | | | | | | |
| <5 cm | | Reference | | | Reference | | |
| ≥5 cm | 1.835 | 1.590-2.119 | <0.001 | 1.115 | 0.954-1.302 | 0.17 | |
| Gastrectomy | | | | | | | |
| Distal | | Reference | | | Reference | | |
| Proximal | 1.035 | 0.875-1.224 | 0.69 | 0.862 | 0.699-1.063 | 0.17 | |
| Total | 1.365 | 1.130-1.648 | 0.001 | 0.895 | 0.713-1.123 | 0.34 | |
| Differentiation | | | | | | | |
| G1 | | Reference | | | Reference | | |
| G2 | 1.680 | 1.117-2.525 | 0.01 | 1.016 | 0.671-1.540 | 0.94 | |
| G3 | 2.731 | 1.841-4.052 | <0.001 | 1.217 | 0.809-1.830 | 0.35 | |
| G4 | 3.240 | 1.776–5.911 | <0.001 | 2.062 | 1.118-3.803 | 0.021 | |
| Γ stage | | | | | | | |
| 1 | | Reference | | | Reference | | |
| 2 | 2.875 | 2.271-3.641 | < 0.001 | 1.633 | 1.262-2.113 | <0.001 | |
| 3 | 3.726 | 2.944-4.716 | < 0.001 | 1.854 | 1.421-2.418 | <0.001 | |
| 4 | 6.622 | 5.114-8.574 | < 0.001 | 3.040 | 2.259-4.092 | <0.001 | |
| N stage | | | | | | | |
| 0 | | Reference | | | Reference | | |
| 1 | 2.696 | 2.226-3.266 | < 0.001 | 2.141 | 1.749–2.621 | <0.001 | |
| 2 | 3.988 | 3.215-4.947 | < 0.001 | 3.152 | 2.503-3.969 | <0.001 | |
| 3 | 5.528 | 4.517-6.766 | < 0.001 | 3.641 | 2.892-4.583 | < 0.001 | |

Table 2 (continued)

Table 2 (continued)

| Variables | Univariate analysis | | | Multivariate analysis | | |
|----------------------------|---------------------|-------------|---------|-----------------------|--------|---------|
| Variables | HR | 95% CI | P value | HR | 95% CI | P value |
| Preoperative radiotherapy | | | | | | |
| No | | Reference | | | | |
| Yes | 1.271 | 0.909-1.778 | 0.16 | | | |
| Preoperative chemotherapy | | | | | | |
| No | | Reference | | | | |
| Yes | 1.071 | 0.832-1.379 | 0.60 | | | |
| Postoperative chemotherapy | | | | | | |
| No | | Reference | | | | |
| Yes | 0.999 | 0.851-1.731 | >0.99 | | | |
| Postoperative radiotherapy | | | | | | |
| No/unknown | | Reference | | | | |
| Yes | 0.849 | 0.687-1.049 | 0.13 | | | |
| ELN | | | | | | |
| <15 | | Reference | | | | |
| ≥15 | 0.930 | 0.805-1.073 | 0.32 | | | |

ELN, examined lymph node; HR, hazard ratio; CI, confidence interval.

Table 3 The univariate and multivariate Cox analysis of overall survival in elderly gastric cancer patients

| Variables – | Univariate analysis | | | Multivariate analysis | | | |
|------------------------------------|---------------------|-------------|---------|-----------------------|-------------|---------|--|
| variables | HR | 95% CI | P value | HR | 95% CI | P value | |
| Age | 1.045 | 1.032–1.058 | <0.001 | 1.030 | 1.016–1.044 | <0.001 | |
| Sex | | | | | | | |
| Female | | Reference | | | Reference | | |
| Male | 0.894 | 0.797-1.004 | 0.059 | 0.787 | 0.698-0.888 | <0.001 | |
| Race | | | | | | | |
| White | | Reference | | | Reference | | |
| Black | 1.028 | 0.850-1.244 | 0.78 | 0.985 | 0.810-1.198 | 0.88 | |
| Asian or Pacific Islander | 0.775 | 0.675-0.890 | <0.001 | 0.723 | 0.627-0.834 | <0.001 | |
| American Indian/Alaska Native | 1.811 | 0.751-4.365 | 0.19 | 1.123 | 0.456-2.768 | 0.80 | |
| Months from diagnosis to treatment | | | | | | | |
| ≤1 month | | Reference | | | Reference | | |
| >1 month | 0.717 | 0.624-0.813 | <0.001 | 0.757 | 0.656-0.827 | <0.001 | |
| Location | | | | | | | |
| Cardia/fundus | | Reference | | | | | |
| Body | 1.004 | 0.818-1.232 | 0.97 | | | | |
| Antrum/pylorus | 0.950 | 0.826-1.092 | 0.47 | | | | |
| Total stomach | 1.137 | 0.910-1.421 | 0.26 | | | | |

Table 3 (continued)

Table 3 (continued)

| Variables | | Univariate analysis | | | Multivariate analysis | | | |
|----------------------------|-------|---------------------|---------|-------|-----------------------|---------|--|--|
| variables | HR | 95% CI | P value | HR | 95% CI | P value | | |
| Tumor size | | | | | | | | |
| <5 cm | | Reference | | | Reference | | | |
| ≥5 cm | 1.422 | 1.265–1.597 | <0.001 | 0.999 | 0.878-1.137 | 0.99 | | |
| Gastrectomy | | | | | | | | |
| Distal | | Reference | | | Reference | | | |
| Proximal | 0.982 | 0.858-1.124 | 0.80 | 1.050 | 0.913-1.209 | 0.49 | | |
| Total | 1.317 | 1.128-1.537 | <0.001 | 1.235 | 1.046-1.458 | 0.01 | | |
| Differentiation | | | | | | | | |
| G1 | | Reference | | | Reference | | | |
| G2 | 1.157 | 0.890-1.504 | 0.28 | 0.938 | 0.715-1.230 | 0.64 | | |
| G3 | 1.620 | 1.258-2.085 | <0.001 | 1.106 | 0.846-1.446 | 0.46 | | |
| G4 | 1.749 | 1.103-2.773 | 0.02 | 1.488 | 0.928-2.385 | 0.10 | | |
| T stage | | | | | | | | |
| 1 | | Reference | | | Reference | | | |
| 2 | 1.873 | 1.598–2.196 | <0.001 | 1.393 | 1.166–1.663 | < 0.001 | | |
| 3 | 2.101 | 1.780-2.480 | <0.001 | 1.627 | 1.335-1.981 | < 0.001 | | |
| 4 | 3.425 | 2.811-4.174 | <0.001 | 2.283 | 1.807-2.884 | < 0.001 | | |
| N stage | | | | | | | | |
| 0 | | Reference | | | Reference | | | |
| 1 | 1.711 | 1.477-1.982 | <0.001 | 1.747 | 1.488-2.051 | < 0.001 | | |
| 2 | 2.480 | 2.088-2.946 | <0.001 | 2.686 | 2.227-3.240 | < 0.001 | | |
| 3 | 3.185 | 2.701-3.756 | <0.001 | 3.345 | 2.744-4.078 | < 0.001 | | |
| Preoperative radiotherapy | | | | | | | | |
| No | | Reference | | | | | | |
| Yes | 1.241 | 0.932-2.654 | 0.14 | | | | | |
| Preoperative chemotherapy | | | | | | | | |
| No | | Reference | | | | | | |
| Yes | 1.025 | 0.828-1.269 | 0.82 | | | | | |
| Postoperative chemotherapy | | | | | | | | |
| No/unknown | | Reference | | | Reference | | | |
| Yes | 0.893 | 0.781-1.020 | 0.09 | 0.653 | 0.547-0.778 | < 0.001 | | |
| Postoperative radiotherapy | | | | | | | | |
| No/unknown | | Reference | | | Reference | | | |
| Yes | 0.826 | 0.697-0.980 | 0.03 | 0.714 | 0.578-0.882 | 0.002 | | |
| ELN | | | | | | | | |
| <15 | | Reference | | | Reference | | | |
| ≥15 | 0.857 | 0.764-0.963 | 0.009 | 0.687 | 0.606-0.779 | <0.001 | | |

ELN, examined lymph node; HR, hazard ratio; CI, confidence interval.

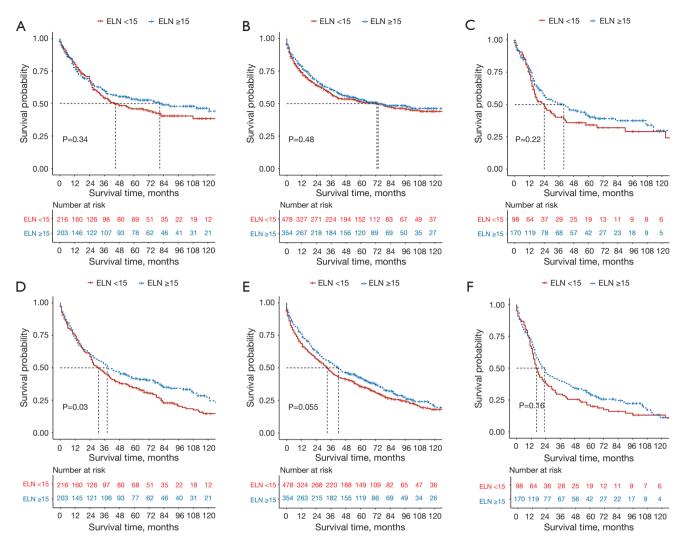


Figure 2 The subgroup Kaplan-Meier survival curve analysis between the two groups according to the gastrectomy type. (A) Cancer-specific survival analysis in the proximal gastrectomy group; (B) cancer-specific survival analysis in the distal gastrectomy group; (C) cancer-specific survival analysis in the total gastrectomy group; (D) overall survival analysis in the proximal gastrectomy group; (E) overall survival analysis in the distal gastrectomy group; (F) overall survival analysis in the total gastrectomy group. ELN, examined lymph node.

time in elderly GC patients, which might indicate that limited lymphadenectomy might be sufficient in elderly GC patients (7,10,11). In contrast, a recent retrospective cohort study demonstrated that the 3-year RFS rate was significantly lower in limited lymphadenectomy group (58.9%) than D2 lymphadenectomy group (80.4%) in elderly GC patients (P=0.047) (8). In the current study, although the OS of D2 lymphadenectomy group was higher than that of limited lymphadenectomy group, no significant difference of CSS was identified between the two groups. Moreover, we found that the difference in OS was only

significant in the proximal gastrectomy group. When we interpret this difference, we must consider the following issues.

Firstly, the elderly patients usually have a shorter life expectancy. At the same time, the underlying health conditions of the elderly patients are also important factors in shortening their life expectancy (12). For elderly GC patients, a Japanese study demonstrated that more than half of patients died from causes other than GC (13). Therefore, considering the impact of comorbidities on postoperative complications and long-term survival of elderly GC patients, careful preoperative evaluation should be done.

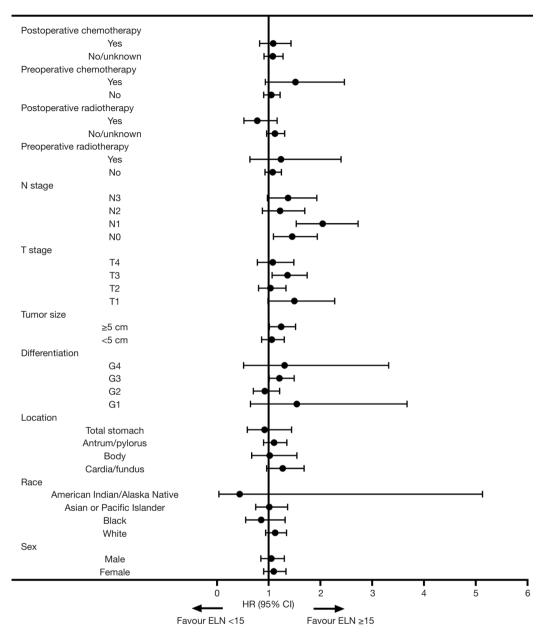


Figure 3 Stratified analysis using important clinical variables to evaluate the impact of limited lymphadenectomy on cancer-specific survival (adjusted by gastrectomy type). ELN, examined lymph node; HR, hazard ratio; CI, confidence interval.

Secondly, postoperative complications are significantly increased in elderly patients (5). It was reported that the incidence of postoperative complications in elderly GC patients was 13–24% (8). Compared with limited lymphadenectomy, D2 lymphadenectomy might increase the risk of postoperative morbidity, reoperation, and mortality in elderly GC patients (7,14). Notably, postoperative complications are also important risk factors

for poor prognosis in GC patients (15,16). Thus, D2 lymphadenectomy should be carefully selected for elderly GC patients.

Thirdly, preoperative neoadjuvant therapy increases the difficulty of lymphadenectomy in elderly GC patients. Previous study has proved that after neoadjuvant chemotherapy, the peri-gastric tissue can produce inflammatory manifestations and cause tissue edema, which increases the difficulty of surgery (17). Our previous study has shown that neoadjuvant chemotherapy toxicity is an independent factor in predicting postoperative complications (18). For the elderly patients, the toxicity of neoadjuvant chemotherapy might further increase the incidence of postoperative complications and prolong the operation time. However, limited lymphadenectomy might reduce this risk to some extent.

Fourthly, the time interval between operation and postoperative adjuvant therapy, as well as the tolerance and completion of adjuvant therapy are closely related with surgical trauma. In clinical practice, compared with limited lymphadenectomy, the expanded surgical scope and high surgical complications of D2 lymphadenectomy will delay the time interval of adjuvant therapy after surgery in elderly GC patients. Besides, there is currently insufficient evidence for the regimen and efficacy of postoperative adjuvant therapy in elderly GC patients. Several clinical trials also excluded elderly GC patients over than 80 years old, when exploring the clinical value of postoperative adjuvant therapy (19,20). In the present study, only 25.23% and 13.15% patients received postoperative chemotherapy and postoperative radiotherapy respectively. Furthermore, according to a questionnaire survey conducted at 58 member institutions of the Stomach Cancer Study Group of the Japan Clinical Oncology Group, a total of 661 GC patients over 80 years old were diagnosed and as stage II and III, and only 248 patients (37.52%) were recommended to receive adjuvant S-1 chemotherapy. However, only 99 patients (14.98%) received adjuvant S-1 chemotherapy (21). Unfortunately, we currently lack studies comparing adjuvant therapy acceptance and prognostic impact after limited lymphadenectomy and D2 lymphadenectomy.

The present study is the first to explore the possibility of limited lymphadenectomy in elderly GC patients through a population-based cohort study. However, several limitations must be admitted and clarified. Firstly, although we included a large number of elderly GC cases, the SEER database is a public database, and many important clinicopathological data are missing, which poses a certain impact on our results. Secondly, due to the lack of surgical safety and short-term postoperative outcomes, such as operation time, intraoperative blood loss, and postoperative complications, the short-term outcomes of limited lymphadenectomy and D2 lymphadenectomy could not be compared. Thirdly, in the process of screening data in the SEER database, there may exist inevitable selection bias, which has a certain impact on the results.

Conclusions

Based on the present study, limited lymphadenectomy might be sufficient for elderly patients with GC. However, prospective studies with a larger sample size are required to validated these results.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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