Characteristics and prognosis of gastric cancer in patients aged ≥ 70 years

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Abstract

AIM: To elucidate the prognostic value of age for gastric cancer and identify the optimal treatment for elderly gastric cancer patients.

METHODS: We enrolled 920 patients with gastric cancer who underwent gastrectomy between January 2003 and December 2007 in our center. Patients were categorized into three groups: younger group (age < 50 years), middle-aged group (50-69 years), and elderly group (≥ 70 years). Clinicopathological features were compared among the three groups and potential prognostic factors were analyzed. The log-rank test was used to assess statistical differences between curves. Independent prognostic factors were identified by the Cox proportional hazards regression model. Stratified analysis was used to investigate the impact of age on survival at each stage. Cancer-specific survival was also compared among the three groups by excluding deaths due to reasons other than gastric cancer. We analyzed the potential prognostic factors for patients aged ≥ 70 years. Finally, the impact of extent of lymphadenectomy and postoperative chemotherapy on survival for each age group was evaluated.

RESULTS: In the elderly group, there was a male predominance. At the same time, cancers of the upper third of the stomach, differentiated type, and less-invasive surgery were more common than in the younger or middle-aged groups. Elderly patients were more likely to have advanced tumor-node-metastasis (TNM) stage and larger tumors, but less likely to have distant metastasis. Although 5-year overall survival (OS) rate specific to gastric cancer was not significantly different among the three groups, elderly patients demonstrated a significantly lower 5-year OS rate than the younger and middle-aged patients (elderly vs middle-aged vs younger patients = 22.0% vs 36.6% vs 38.0%, respectively). In the TNM-stratified analysis, the differences in OS were only observed in patients with II and III tumors. In multivariate analysis, only surgical margin status, pT4, lymph node metastasis, M1 and sex were independent prognostic factors for elderly patients. The 5-year OS rate did not differ between elderly patients undergoing D1 and D2 lymph node resection, and these patients benefited little from chemotherapy.

CONCLUSION: Age ≥ 70 years was an independent prognostic factor for gastric cancer after gastrectomy. D1 resection is appropriate and postoperative chemotherapy is possibly unnecessary for elderly patients with gastric cancer.
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INTRODUCTION

The population of China is growing both larger and older. According to the National Bureau of Statistics of China (NBSC, 2011), the population of China reached 1.35 billion at the end of 2011, making it the most populous country in the world, and the number of people aged ≥65 years has risen to 118 million, or approximately 8.87% of the total population compared to 6.96% in 2000. With the aging of the population, the number of patients aged ≥70 years with gastric cancer is increasing in China. It has been reported that surgery is safe and the surgical outcome is better compared with the best supportive care in elderly gastric cancer patients[1,2]. However, it is still unclear whether surgical outcome in elderly patients differs from that in younger patients. In Japan, treatment guidelines for gastric cancer have been issued, and a standard therapeutic strategy for gastric cancer by stage has been established. Gastrectomy with D2 lymph node dissection has been increasingly regarded as the standard surgical procedure for most patients with operable gastric cancer. For elderly patients, it is not established whether these therapeutic strategies are suitable and controversy still exits. Previous studies have compared outcomes between elderly and younger patients with gastric cancer[3,4]. However, gastric cancer in younger patients also has distinctive properties.

In the present study, we compared the clinicopathological characteristics and surgical outcomes of gastric cancer among elderly patients (≥70 years), middle-aged patients (50-69 years), and younger patients (< 50 years). Our ultimate aim was to identify the optimal treatment for elderly patients with gastric cancer.

MATERIALS AND METHODS

Patients

We reviewed surgical and pathological data of 920 patients with gastric cancer who had undergone gastrectomy with lymph node dissection, who were followed up between January 2003 and December 2007 at Tianjin Medical University Cancer Institute and Hospital. All the patients had histologically confirmed gastric adenocarcinoma. Patients who had previously undergone gastric surgery or had received neoadjuvant chemotherapy were excluded. There were 659 men (71.6%) and 261 women (28.4%), with a median age of 62 years (age range: 20-89 years). All the patients were categorized into the following three groups: younger group (< 50 years old, 166 patients), middle-aged group (50-69 years old, 481 patients) and elderly group (≥ 70 years, 273 patients).

Surgical treatment and perioperative management

All the patients underwent gastrectomy with D1 or D2 lymph node dissection. The choice of surgical procedure of reconstruction was made according to the surgeon’s preference. Resection margin was detected by histological examination. Positive resection margin was defined as microscopic complete resection, without residual cancer cells in the margin. Postoperative adjuvant chemotherapy was implemented according to the tumor stage, physical condition and willingness of the patient. Chemotherapeutics consisted of 5-fluorouracil, leucovorin and oxaliplatin (FOLFOX-6). Radiotherapy was not used in the present study.

Evaluation of clinicopathological variables and survival

Clinicopathological features studied included sex, age, tumor location, tumor size, Borrmann type, histology, surgical margin status, extranodal metastasis, depth of invasion, lymph node metastasis, distant metastasis, tumor-node-metastasis (TNM) stage, extent of lymphadenectomy, type of gastrectomy, and postoperative chemotherapy. The tumors were staged according to the Union for International Cancer Control TNM classification system, 7th edition, and lymphadenectomy and lymph node stations were defined according to the 3rd English Edition of the Japanese Classification of Gastric Carcinoma. Tumors were classified into two groups based on histology: differentiated type, including papillary, well or moderately differentiated adenocarcinoma; and undifferentiated type, including poorly differentiated or undifferentiated adenocarcinoma, signet ring cell carcinoma and mucinous carcinoma.

Follow-up

All the patients were followed every 3 mo until 2 years...
after surgery, then every 6 mo for up to 5 years, and then every year or until death. Physical examination, laboratory tests, imaging and endoscopy were performed at every visit. The median follow-up was 26 mo (range: 1-103 mo), and the last follow-up date was December 25, 2012. The overall survival rate was calculated from the day of surgical resection until time of death or final follow-up.

Statistical analysis
Categorical variables were analyzed by means of the $\chi^2$ or Fisher’s exact test. Overall survival curves were calculated using the Kaplan-Meier method based on the length of time between primary surgical treatment and final follow-up or death. The log-rank test was used to assess statistical differences between curves. Independent prognostic factors were identified by Cox proportional hazards regression model. $P < 0.050$ was considered statistically significant. The statistical analysis was performed using SPSS version 17.0 (Chicago, IL, United States).

RESULTS
Clinicopathological features
Of the 920 patients who underwent gastrectomy, 793 patients achieved a negative resection margin (241 elderly, 415 middle-aged and 137 younger patients), and 127 patients had a positive resection margin (32 elderly, 66 middle-aged and 29 younger patients). Of all the patients, 402 (43.7%) underwent D2 lymph nodes dissection, and 518 (56.3%) D1 dissection, including 65 (7.1%) patients who accepted palliative surgery without formal lymph node dissection because of distant metastasis. Six hundred and seventy-one (72.9%) patients accepted surgery alone and 249 (27.1%) surgery plus postoperative chemotherapy with FOLFOX-6.

All the patients were divided into three categories according to their age (Table 1). The mean age was 42.8 years in the younger group, 60.1 years in the middle-aged group, and 74.1 years in the elderly group. There were no significant differences in Borrmann type, extranodal metastasis, surgical margin status, depth of invasion, and lymph node metastasis among the three groups. In the elderly group, there was a male predominance, and cancers of the upper third of the stomach and differentiated type, and less-invasive surgery were more common than in the younger and middle-aged groups. The elderly patients were more likely to have advanced TNM stage and larger tumors, but less likely to have distant metastasis and undergo postoperative chemotherapy. The rate of distant metastasis was 10.2% in the younger group, 8.1% in the middle-aged group, and 3.3% in the elderly group. Although there were no significant differences in type of distant metastasis, elderly patients were more likely to have liver metastasis, but less likely to have peritoneal metastasis than younger or middle-aged patients.

Prognostic value of age in gastric cancer
The results of univariate and multivariate analysis of all 920 patients are shown in Table 2. Surgical margin status, pT, N stage, M1, extent of lymphadenectomy, postoperative chemotherapy and age $\geq$ 70 years (hazard ratio: 1.487, $P = 0.003$) remained as independent prognostic factors for overall survival (OS). Patients aged $\geq$ 70 years demonstrated a significantly lower 5-year OS rate than the younger and middle-aged patients (elderly vs middle-aged vs younger patients, 22.0% vs 36.6% vs 38.0%, respectively) (Figure 1). In the TNM-stratified analysis, the differences in OS were only observed in patients with TNM stage II and III cancer (Table 3 and Figure 2). However, when deaths caused by factors other than gastric cancer were excluded, there were no significant differences in cancer-specific survival among the three groups (Figure 3).

Survival of patients aged $\geq$ 70 years
Survival analysis of the elderly patients is shown in Table 4. Sex, tumor size, histology, extranodal metastasis, surgical margin status, pT, lymph node metastasis, M1 and type of gastrectomy were found to be prognostic factors in the univariate analysis, while only surgical margin status, pT, lymph node metastasis, M1 and sex were independent prognostic factors in the multivariate analysis. For patients aged $\geq$ 70 years, women tended to have a significantly higher 5-year OS than men (29.3% vs 20.0%, $P = 0.045$). Although the patients who underwent D2 resection had better survival than those with D1 resection, there was no significant difference in OS between D1 and D2 resection for the elderly patients. In the stratified analysis, chemotherapy was a prognostic factor for the younger and middle-aged patients, but not for the elderly patients (Table 5 and Figure 4).

DISCUSSION
The number of elderly patients with gastric cancer is rapidly increasing with an aging population. With regard to elderly, no clear-cut distinction exists. Previous studies used 65, 70, 75, 80 and 85 years as thresholds[1-7]. Data from NBSC show that the average life span in China was 72.38 years for men and 77.37 years for women in 2010, and patients aged $\geq$ 65 years accounted for 8.87% of the total population. Taking into consideration that the majority of elderly patients with gastric cancer are male, we used 70 years as a threshold, which is close to the average life span of Chinese men. Many elderly patients with gastric cancer also suffer from comorbid diseases such as hypertension, diabetes mellitus, ischemic heart disease, brain infarction, or renal dysfunction. Therefore, we have to treat elderly patients individually with particular care. Gastric cancer in elderly patients actually presents a distinctive entity with specific clinicopathological characteristics.

The current study showed that the distinguishing characteristics in the elderly gastric cancer patients included male predominance, more histologically differentiated type, higher rate of tumors located in the upper third of the stomach, larger tumor size, more advanced
Many studies have shown a male predominance in elderly gastric cancer patients [8,9], and in younger patients (< 40 years), the sex ratio has been reported to be ap-

Table 1  Case characteristics  \( n (\%) \)

| Characteristics          | \(<\ 50\ (n\ =\ 166)\) | \(50-69\ (n\ =\ 481)\) | \(\geq\ 70\ (n\ =\ 273)\) | \(\chi^2\) | \(P\) value |
|--------------------------|--------------------------|--------------------------|--------------------------|------------|------------|
| Age (mean ± SD)          | 42.8 ± 5.8               | 60.1 ± 5.5               | 74.1 ± 3.4               |            |            |
| Gender                   |                          |                          |                          | 32.504     | < 0.001    |
| Female                   | 76 (45.8)                | 127 (26.4)               | 58 (21.2)                |            |            |
| Male                     | 90 (54.2)                | 354 (73.6)               | 215 (78.8)               |            |            |
| Tumor location           |                          |                          |                          | 39.900     | < 0.001    |
| Lower 1/3                | 83 (50.0)                | 201 (41.8)               | 88 (40.4)                |            |            |
| Middle 1/3               | 31 (18.7)                | 87 (18.1)                | 48 (17.6)                |            |            |
| Upper 1/3                | 21 (12.7)                | 143 (29.7)               | 106 (38.8)               |            |            |
| 2/3 or more              | 31 (18.7)                | 50 (10.4)                | 31 (11.4)                |            |            |
| Tumor location           |                          |                          |                          | 34.186     | < 0.001    |
| Upper 1/3                | 21 (12.7)                | 143 (29.7)               | 106 (38.8)               |            |            |
| Non-upper 1/3           | 145 (87.3)               | 338 (70.3)               | 167 (61.2)               |            |            |
| Tumor size               |                          |                          |                          | 13.589     | 0.001      |
| < 5 cm                   | 79 (47.6)                | 209 (43.5)               | 87 (31.9)                |            |            |
| ≥ 5 cm                   | 87 (52.4)                | 272 (56.5)               | 186 (68.1)               |            |            |
| Tumor size, cm (mean ± SD)| 5.640 ± 3.172           | 5.552 ± 2.810            | 6.304 ± 3.644            |            |            |
| Borrmann type            |                          |                          |                          | 2.443      | 0.296      |
| I / II                   | 47 (28.3)                | 166 (34.5)               | 95 (34.8)                |            |            |
| III / IV                 | 119 (71.7)               | 315 (65.5)               | 178 (65.2)               |            |            |
| Histology                |                          |                          |                          | 39.366     | < 0.001    |
| Differentiated           | 24 (14.5)                | 139 (28.9)               | 116 (42.5)               |            |            |
| Undifferentiated         | 142 (85.5)               | 342 (71.1)               | 157 (57.5)               |            |            |
| Extranodal metastasis    |                          |                          |                          | 4.733      | 0.094      |
| Negative                 | 121 (72.9)               | 378 (78.6)               | 223 (81.7)               |            |            |
| Positive                 | 45 (27.1)                | 103 (21.4)               | 50 (18.3)                |            |            |
| Surgical margin status   |                          |                          |                          | 2.873      | 0.238      |
| Negative                 | 137 (82.5)               | 415 (86.3)               | 241 (88.3)               |            |            |
| Positive                 | 29 (17.5)                | 66 (13.7)                | 32 (11.7)                |            |            |
| Depth of invasion        |                          |                          |                          | 5.457      | 0.487      |
| pT1                      | 4 (2.4)                  | 12 (2.5)                 | 6 (2.2)                  |            |            |
| pT2                      | 22 (13.3)                | 49 (10.2)                | 22 (8.1)                 |            |            |
| pT3                      | 5 (3.0)                  | 30 (6.2)                 | 17 (6.2)                 |            |            |
| pT4                      | 135 (81.3)               | 390 (81.1)               | 228 (83.5)               |            |            |
| Lymph node metastasis    |                          |                          |                          | 5.325      | 0.503      |
| pN0                      | 62 (37.3)                | 170 (35.5)               | 87 (31.9)                |            |            |
| pN1                      | 26 (15.7)                | 83 (17.3)                | 51 (18.7)                |            |            |
| pN2                      | 32 (19.3)                | 108 (22.5)               | 73 (26.7)                |            |            |
| pN3                      | 46 (27.7)                | 120 (24.9)               | 62 (22.7)                |            |            |
| Distant metastasis       |                          |                          |                          | 9.251      | 0.010      |
| M0                       | 149 (89.8)               | 442 (91.9)               | 264 (96.7)               |            |            |
| M1                       | 17 (10.2)                | 39 (8.1)                 | 9 (3.3)                  |            |            |
| Types of distant metastasis |                      |                          |                          | 5.502      | 0.240      |
| Liver metastasis         | 5 (29.4)                 | 19 (48.7)                | 5 (55.6)                 |            |            |
| Peritoneal metastasis    | 12 (70.6)                | 18 (51.3)                | 3 (33.3)                 |            |            |
| Other distant metastasis | 0 (0.0)                  | 2 (5.1)                  | 1 (11.1)                 |            |            |
| TNM stage                |                          |                          |                          | 13.270     | 0.039      |
| I                        | 19 (11.4)                | 43 (8.9)                 | 21 (7.7)                 |            |            |
| II                       | 45 (27.1)                | 135 (28.1)               | 72 (26.4)                |            |            |
| III                      | 85 (51.2)                | 264 (54.9)               | 171 (62.6)               |            |            |
| IV                       | 17 (10.2)                | 39 (8.1)                 | 9 (3.3)                  |            |            |
| Chemotherapy             |                          |                          |                          | 48.852     | < 0.001    |
| Yes                      | 71 (42.8)                | 142 (29.5)               | 36 (13.2)                |            |            |
| No                       | 95 (57.2)                | 339 (70.5)               | 237 (86.8)               |            |            |
| Type of gastrectomy      |                          |                          |                          | 7.466      | 0.024      |
| Subtotal                 | 112 (67.5)               | 361 (75.1)               | 216 (79.1)               |            |            |
| Total                    | 54 (32.5)                | 120 (24.9)               | 57 (20.9)                |            |            |
| Extent of lymphadenectomy|                          |                          |                          | 19.735     | < 0.001    |
| D2                       | 89 (53.6)                | 222 (46.2)               | 91 (33.3)                |            |            |
| D1                       | 77 (46.4)                | 259 (53.8)               | 182 (66.7)               |            |            |

TNM stage, and less distant metastasis compared to the younger and middle-aged patients. Also in the elderly group, subtotal gastrectomy and D1 resection were more frequently performed, while few patients underwent postoperative chemotherapy.

Many studies have shown a male predominance in elderly gastric cancer patients [8,9], and in younger patients (< 40 years), the sex ratio has been reported to be ap-
proximately 1:1\textsuperscript{[10]}. Our findings are consistent with these reports. The sexual imbalance may reflect a more frequent and prolonged exposure of elderly male patients to environmental carcinogens. We also found that the proportion of the histologically differentiated type cancer increased with aging, from 14.5% in the younger patients to 42.5% in the elderly. Some studies concluded that gastric carcinoma in elderly patients may principally develop as well-differentiated lesions that progress to poorly differentiated ones, whereas in younger patients, most gastric carcinoma emerges as poorly differentiated type at an early phase\textsuperscript{[11,12]}. This may also be attributed to the fact that younger patients are more likely to have distant metastasis. Although many studies have demonstrated that gastric cancer in elderly patients was predominantly localized in the lower third of the stomach\textsuperscript{[8,11,12]}, some researchers reported that cancer involving the upper third of the stomach was more common in elderly than in younger patients\textsuperscript{[13,14]}. In our study, only 28.6% of tumors were located in the lower third of the stomach in elderly patients, and the ratio of upper-third tumors increased from 12.7% in the younger patients to 38.8% in the el-

### Table 2  Survival analysis of all patients with gastric cancer after surgery

| Characteristics          | n (%) | 5-yr OS | MST (mo) | Univariate analysis | Multivariate analysis |
|--------------------------|-------|---------|----------|---------------------|-----------------------|
|                          |       |         |          | \( \chi^2 \)        | \( P \) (log-rank)    |
|                          |       |         |          | Hazard ratio (95%CI) | \( P \) value         |
| Gender                   |       |         |          |                     |                       |
| Male                     | 659 (71.6) | 32.00% | 26       | 0.165               | 0.685                 |
| Female                   | 261 (28.4) | 33.70% | 27       |                     |                       |
| Age (yr)                 |       |         |          |                     |                       |
| < 50                     | 166 (18.0) | 36.00% | 32       | 21.067 \* < 0.000   | 1 (ref)               |
| 50-69                    | 481 (52.3) | 36.60% | 28       | 1.107 (0.881, 1.391) | 0.383                 |
| \( \geq 70 \)            | 273 (29.7) | 22.00% | 20       | 1.487 (1.149, 1.924) | 0.003                 |
| Tumor location           |       |         |          |                     |                       |
| Lower 1/3                | 372 (40.4) | 40.10% | 36       | 1 (ref)             |                       |
| Middle 1/3               | 166 (18.0) | 30.10% | 28       | 1.129 (0.881, 1.446) | 0.339                 |
| Upper 1/3                | 270 (29.3) | 29.60% | 25       | 1.063 (0.864, 1.309) | 0.564                 |
| 2/3 or more              | 112 (12.2) | 17.90% | 16       | 1.311 (0.985, 1.744) | 0.064                 |
| Tumor size               |       |         |          |                     |                       |
| < 5 cm                   | 375 (40.8) | 45.10% | 42       | 1 (ref)             |                       |
| \( \geq 5 \) cm          | 545 (59.2) | 23.90% | 20       | 1.185 (0.994, 1.413) | 0.058                 |
| Borrmann type            |       |         |          |                     |                       |
| I / II                   | 308 (33.5) | 38.30% | 33       | 1 (ref)             |                       |
| III / IV                 | 612 (66.5) | 29.60% | 23       | 1.171 (0.980, 1.399) | 0.082                 |
| Histology                |       |         |          |                     |                       |
| Differentiated           | 279 (30.3) | 41.20% | 34       | 1 (ref)             |                       |
| Undifferentiated         | 641 (69.7) | 28.70% | 23       | 1.201 (0.996, 1.449) | 0.055                 |
| Extramodal metastasis    |       |         |          |                     |                       |
| Negative                 | 722 (78.5) | 37.10% | 31       | 1 (ref)             |                       |
| Positive                 | 198 (21.5) | 15.70% | 15       | 1.164 (0.962, 1.409) | 0.119                 |
| Surgical margin status   |       |         |          |                     |                       |
| Negative                 | 793 (86.2) | 36.70% | 31       | 1 (ref)             |                       |
| Positive                 | 127 (13.8) | 6.30%  | 11       | 1.705 (1.357, 2.142) | < 0.001               |
| Depth of invasion        |       |         |          |                     |                       |
| pT1                      | 22 (2.4) | 86.40% | 69       | 67.084 \* < 0.001   | 1 (ref)               |
| pT2                      | 93 (10.4) | 61.30% | 61       | 3.048 (0.937, 9.918) | 0.064                 |
| pT3                      | 52 (5.7) | 46.20% | 47       | 3.188 (0.965, 10.526) | 0.057                 |
| pT4                      | 753 (81.8) | 26.40% | 21       | 4.580 (1.431, 14.200) | 0.010                 |
| Lymph node metastasis    |       |         |          |                     |                       |
| pN0                      | 319 (34.7) | 57.70% | 24       | 1 (ref)             |                       |
| pN1                      | 160 (17.4) | 31.90% | 24       | 1.713 (1.327, 2.211) | < 0.001               |
| pN2                      | 213 (23.2) | 25.30% | 23       | 1.918 (1.514, 2.429) | < 0.001               |
| pN3                      | 228 (24.8) | 6.10%  | 13       | 3.268 (2.572, 4.151) | < 0.001               |
| Distant metastasis       |       |         |          |                     |                       |
| M0                       | 855 (92.9) | 34.70% | 29       | 1 (ref)             |                       |
| M1                       | 65 (7.0) | 3.10%  | 8        | 1.817 (1.339, 2.465) | < 0.001               |
| Chemotherapy             |       |         |          |                     |                       |
| Yes                      | 249 (27.1) | 39.80% | 37       | 1 (ref)             |                       |
| No                       | 671 (72.9) | 29.80% | 22       | 1.383 (1.144, 1.673) | 0.001                 |
| Type of gastrectomy      |       |         |          |                     |                       |
| Subtotal                 | 689 (73.9) | 36.90% | 31       | 1 (ref)             |                       |
| Total                    | 231 (26.1) | 19.50% | 16       | 1.170 (0.944, 1.450) | 0.151                 |
| Extent of lymphadenectomy|       |         |          |                     |                       |
| D2                       | 402 (43.7) | 36.60% | 28       | 4.060 0.044         | 1 (ref)               |
| D1                       | 518 (56.3) | 29.30% | 24       | 1.192 (1.005, 1.414) | 0.043                 |

Ref: Reference category; OS: Overall survival; MST: Median survival time.
When deaths caused by factors other than gastric cancer were excluded, there were no significant differences in cancer-specific survival among the three age groups. EG: Elderly group; MG: Middle-aged group; YG: Younger group.

Figure 1 Overall survival curves for all patients grouped by age. Patients aged ≥70 years demonstrated a significantly lower 5-year OS rate than the younger and middle-aged patients (elderly vs middle-aged vs younger patients, 22.0% vs 36.6% vs 38.0%, respectively). EG: Elderly group; MG: Middle-aged group; YG: Younger group.

Figure 2 Overall survival curves for patients with tumor-node-metastasis stage II and III cancer. In the tumor-node-metastasis (TNM)-stratified analysis, the differences in overall survival (OS) were only observed in patients with TNM stage II and III cancer. A: Patients with II cancer; B: Patients with III cancer. EG: Elderly group; MG: Middle-aged group; YG: Younger group.

Figure 3 Cancer-specific survival of each age group. When deaths caused by factors other than gastric cancer were excluded, there were no significant differences in cancer-specific survival among the three age groups. EG: Elderly group; MG: Middle-aged group; YG: Younger group.

derly patients. It is possible that the risk of developing carcinoma in the upper third of the stomach increases with advancing age. Previous reports have shown no significant difference in tumor stage between elderly and younger or middle-aged patients\(^{[15,17]}\). Although in the present study there were no significant differences in the depth of invasion and lymph node metastasis among the three groups, the elderly patients were more likely to have advanced TNM stage. The ratio of stage III cancer was 62.6% in the elderly patients compared to 51.2% in the younger patients. Usually the symptoms of gastric cancer are not obvious in elderly patients, which may result in delayed diagnosis. Thus, it is easier for advanced tumor stage and larger tumor size to develop in elderly than younger and middle-aged patients.

It has been reported that surgery is safe and surgical outcome is better compared with the best supportive care in elderly patients with gastric cancer.\(^{[15,18]}\). Limited operation is predominant because total gastrectomy and D2 resection in elderly patients are associated with higher rates of postoperative morbidity and mortality compared to subtotal gastrectomy and D1 resection\(^{[15,18]}\). In the present study, subtotal gastrectomy and D1 resection were more frequently performed in the elderly patients. However, the long-term outcome of elderly patients is still controversial after limited operation.

Many studies have specifically compared the long-term outcome of gastric cancer in elderly patients with that in younger or middle-aged patients. Some found no significant difference in survival between them\(^{[15,19]}\). However,
ever, most studies confirmed the prognosis of elderly patients was poorer than that of younger and middle-aged patients\[8,16,22,23\]. Our results are consistent with most of those reports. Patients aged ≥ 70 years had a significantly lower 5-year OS rate than younger and middle-aged patients. In general, the poor prognosis of elderly patients can be attributed to the delay in diagnosis and advanced tumor stage\[21\]. However, in TNM-stratified analysis, such differences were still observed in stage II and III cancer. In multivariate analysis, age was an independent prognostic factor, as well as surgical margin status, pT, lymph node metastasis, M1, chemotherapy and the extent of lymphadenectomy. It has been reported that as patients age, they have a reduced ability to tackle cancer growth, which may lead to poorer prognosis of elderly patients\[21\]. In our study, when deaths caused by other comorbid diseases and malignancies were excluded, there were no significant differences in cancer-specific survival among the three groups. This result agrees with previous studies\[8,17,22,23\]. According to our results, the poorer prognosis of the elderly patients with gastric cancer was due to other comorbid diseases and malignancies rather than gastric cancer itself. To improve the outcome of gastric cancer in elderly patients, we should pay attention to treating other comorbid diseases and malignancies in addition to providing adequate treatment for gastric cancer itself.

Elderly patients have distinguishing characteristics and prognosis from younger and middle-aged ones, thus, it is necessary to elucidate prognostic factors that influence OS in elderly patients. In the present study, sex, surgical margin status, pT, lymph node metastasis and M1 disease were found to be independent prognostic factors for elderly patients with gastric cancer. Some studies have reported better prognosis for women than men\[24,25\]. Usually, women have a longer life-span than men. In 2005, life expectancy was 2.4 years longer for women than men in India, 3.2 years longer in China, 3.8 years longer in Indonesia, and 7.4 years longer in Japan\[26\]. This may account for the better prognosis of female elderly patients with gastric cancer. Depth of invasion, lymph node status and distant metastasis have been proven to be the most powerful independent prognostic factors for gastric cancer. However, few studies have specifically evaluated the prognostic value of these factors in elderly patients. Yokota et al\[27\] reported that lymph node metastasis and depth of invasion were significantly correlated with 5-year survival in patients aged > 70 years. Pisanu et al\[28\] demonstrated that tumor stage was the only prognostic factor influencing survival for patients aged ≥ 75 years. Our results were consistent with these reports and strongly showed that depth of invasion, lymph node metastasis and M1 disease were independent prognostic factors for elderly patients. R0 resection represents the only treatment modality offering possible long-term survival. Positive surgical margin status has been reported to be associated with poor prognosis in patients with gastric cancer\[29,30\]. Our results showed that surgical margin was an independent prognostic factor for all the patients including elderly ones. To ensure a negative surgical margin

Figure 4  Overall survival curves for patients grouped by chemotherapy. In the age-stratified analysis, chemotherapy was a prognostic factor for the younger and middle-aged patients, but not for the elderly patients. A: All patients; B: Younger group; C: Middle-aged group; D: Elderly group.

Liang YX et al. Age and gastric cancer
is of paramount importance in gastric cancer surgery. Extended lymphadenectomy (D2) has been reported to yield better survival results in Asian countries, such as Japan and Korea where gastric carcinoma is very common. Until the 15-year follow-up results of the randomized Dutch D1D2 trial were published, D2 was not recommended in western countries. The follow-up data showed that OS of patients who had curative resection

| Table 4 | Survival analysis of gastric cancer patients aged ≥ 70 years |
| --- | --- |
| Characteristics | n (%) | 5-yr OS | MST (mo) | Univariate analysis | Multivariate analysis | Ref: Reference category; OS: Overall survival; MST: Median survival time. |
| Gender | | | | | $z^2$ | $P$ (log-rank) | Hazard ratio (95%CI) | $P$ value |
| Female | 58 (21.2) | 29.30% | 31 | 4.009 | 0.045 | 1 (ref) |
| Male | 215 (78.8) | 20.00% | 18 | 1.433 (1.013, 2.029) | 0.042 |
| Age (yr) | | | | | | | | |
| < 75 | 164 (60.1) | 23.20% | 20 | 0.092 | 0.762 |
| ≥ 75 | 109 (39.9) | 20.20% | 19 | 6.055 | 0.109 |
| Tumor location | | | | | | | | |
| Lower 1/3 | 78 (28.6) | 25.60% | 22 | 1.119 (0.816, 1.533) | 0.099 |
| Middle 1/3 | 58 (21.2) | 22.40% | 15 | 1.272 (0.956, 1.693) | 0.225 |
| Upper 1/3 | 106 (38.8) | 21.70% | 22 | 1.433 (1.013, 2.029) | 0.042 |
| 2/3 or more | 31 (11.4) | 12.90% | 16 | 1.119 (0.816, 1.533) | 0.485 |
| Tumor size | | | | | | | | |
| < 5 cm | 87 (31.9) | 32.20% | 31 | 3.221 | 0.073 |
| ≥ 5 cm | 186 (68.1) | 17.20% | 17 | 1.248 (0.873, 1.784) | 0.029 |
| Borrmann type | | | | | | | | |
| I / II | 95 (34.8) | 27.40% | 26 | 1.658 (1.048, 2.391) | 0.007 |
| III / IV | 178 (65.2) | 19.10% | 18 | 1.583 (1.048, 2.391) | 0.029 |
| Histology | | | | | | | | |
| Differentiated | 116 (42.5) | 28.40% | 23 | 2.332 (1.143, 4.756) | 0.020 |
| Undifferentiated | 157 (57.5) | 17.20% | 18 | 1.248 (0.873, 1.784) | 0.004 |
| Extraregional metastasis | | | | | | | | |
| Negative | 223 (81.7) | 25.60% | 22 | 1.305 (0.936, 1.820) | 0.117 |
| Positive | 45 (18.3) | 10.00% | 11 | 1.658 (1.048, 2.334) | 0.004 |
| Surgical margin status | | | | | | | | |
| Negative | 241 (88.3) | 24.10% | 22 | 1.773 (1.118, 2.811) | 0.015 |
| Positive | 32 (11.7) | 6.30% | 12 | 1.773 (1.118, 2.811) | 0.015 |
| Depth of invasion | | | | | | | | |
| pT1 | 45 (16.5) | 51.10% | 65 | 20.751 | 0.001 |
| pT2 | 228 (83.5) | 16.20% | 17 | 20.751 | 0.001 |
| pN0 | 87 (31.9) | 40.20% | 44 | 3.097 | 0.001 |
| pT1-N1 | 186 (68.1) | 13.40% | 16 | 1.658 (1.048, 2.334) | 0.004 |
| Lymph node metastasis | | | | | | | | |
| M0 | 264 (96.7) | 22.70% | 21 | 2.332 (1.143, 4.756) | 0.020 |
| M1 | 9 (3.3) | 0.00% | 6 | 0.008 | 0.476 |
| Chemotherapy | | | | | | | | |
| Yes | 36 (13.2) | 13.90% | 20 | 0.508 | 0.476 |
| No | 237 (86.8) | 23.20% | 20 |
| Type of gastrectomy | | | | | | | | |
| Subtotal | 214 (78.4) | 24.80% | 22 | 1.135 (0.936, 1.380) | 0.225 |
| Total | 59 (21.6) | 11.90% | 14 | 1.135 (0.936, 1.380) | 0.225 |
| Extent of lymphadenectomy | | | | | | | | |
| D2 | 91 (33.3) | 19.80% | 17 | 1.429 | 0.232 |
| D1 | 182 (66.7) | 23.10% | 22 |

| Table 5 | Comparison of survival rate for patients treated with chemotherapy or not stratified by age |
| --- | --- |
| Age (yr) | Yes | Chemotherapy | No | Yes | Chemotherapy | $z^2$ | $P$ value |
| | n | 5-yr OS | MST (mo) | n | 5-yr OS | MST (mo) |
| < 50 | 71 | 47.90% | 53 | 47.90% | 53 | 8.774 | 0.003 |
| 50-69 | 142 | 42.30% | 37 | 339 | 34.20% | 22 | 7.427 | 0.006 |
| ≥ 70 | 36 | 13.90% | 20 | 237 | 23.20% | 20 | 0.508 | 0.476 |

OS: Overall survival; MST: Median survival time.
was 25% for D1 and 35% for D2 when postoperative deaths (4% in D1 and 10% in D2) were excluded (log-rank \( P = 0.08 \)), however, there were no significant differences in survival between D1 and D2 for patients \( \geq 70 \) years of age (3% for D1 and 13% for D2, \( P = 0.36 \))\[19,20]\). Also the 5-year follow-up results from the Dutch Gastric Cancer Trial showed no significant survival benefit in the D2 group (47% for D2 and 45% for D1)\[21]\). In elderly patients, surgeons are usually reluctant to perform D2 resection to avoid major complications in the postoperative period\[21,22]\). It was actually reported that none of the elderly patients had lymph node recurrence following limited lymph-node resection\[21]\). In our study, there were no significant differences in OS between D1 and D2 resection for patients aged \( \geq 70 \) years (5-year OS: 23.1% for D1 and 19.8% for D2, \( P = 0.232 \)), although those aged < 70 years may benefit from D2 resection. The average life expectancy of elderly patients is short, which may obscure the value of D2 resection, and explain why it is of little benefit in elderly patients. Considering this rather short life expectancy and the increased risk for D2 resection in elderly patients, D1 may be an adequate procedure for elderly patients with gastric cancer.

Many studies have affirmed the survival benefit with postoperative chemotherapy or chemoradiotherapy for gastric cancer\[23-30]\). However, no clinical trial has demonstrated that elderly patients can benefit from postoperative chemotherapy. Although the Adjuvant Chemotherapy of TS-1 for Gastric Cancer (ACTS GC) trial in Japan showed that 3-year survival rates were 80.1% and 70.1% for patients treated with S-1 or surgery alone, respectively, the results concerning elderly patients was not statistically significant\[29]. FOLFOX-6 has been widely used in gastric cancer patients and has equal efficacy to the XELOX regimen (capecitabine/oxaliplatin), which improved 3-year disease-free survival in the CLASSIC (Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy) trial\[31]\). In our study, improved survival with chemotherapy was only observed in the younger and middle-aged patients, and elderly patients benefited little from chemotherapy. Only 36 (13.2%) elderly patients received postoperative chemotherapy in the present study, therefore, we could not draw any definitive conclusions. A multicenter, larger study is recommended for future investigations.

In conclusion, patients aged \( \geq 70 \) years had distinctive characteristics such as male predominance, larger tumor size, more histological differentiated type, higher rate of tumors located in the upper third of the stomach, and advanced TNM stage, but less distant metastasis compared to younger and middle-aged patients. Although there was no significant difference in the prognosis specific to gastric cancer, the elderly patients demonstrated poorer prognosis than the younger and middle-aged patients. Age \( \geq 70 \) years was an independent prognostic factor for patients with gastric cancer after gastrectomy. Considering short life expectancy, limited lymph node dissection (D1 resection) is appropriate and postoperative chemotherapy is possibly unnecessary for elderly patients.

**COMMENTS**

**Background**

The population of China is growing both larger and older. With the aging of the population, the number of patients aged \( \geq 70 \) years with gastric cancer is also increasing. However, it is still unclear whether elderly patients benefit from adjuvant chemotherapy or extended lymph-node dissection.

**Research frontiers**

Gastrectomy with D2 lymph node dissection has been increasingly regarded as the standard surgical procedure for most patients with operable gastric cancer, and postoperative adjuvant chemotherapy can improve overall survival. However, it is still controversial whether these therapeutic strategies are suitable for elderly patients. In the present study, authors demonstrated that age \( \geq 70 \) years is an independent prognostic factor for patients with gastric cancer after gastrectomy, D1 resection is appropriate, and postoperative chemotherapy is possibly unnecessary for elderly patients.

**Innovations and breakthroughs**

Few studies have compared the characteristics and prognosis of gastric cancer among younger, middle-age and elderly patients. In this study, authors compared characteristics and prognosis among the three age groups and found that elderly patients had distinctive characteristics such as male predominance, larger tumor size, more histological differentiated type, higher rate of tumors located in the upper third of the stomach, and advanced tumor-node-metastasis stage, but less distant metastasis compared to younger and middle-aged patients. Furthermore, cancer-specific survival was almost equal between the elderly and the younger patients, but overall mortality was higher in the former group.

**Applications**

By understanding the characteristics and prognostic factors of elderly gastric cancer patients, this study may provide a reference for treatment planning for elderly patients with gastric cancer in China.

**Terminology**

Extranodal metastasis was defined as the presence of tumor cells in extramural soft tissue that was discontinuous with either the primary lesion or locoregional lymph nodes.

**Peer review**

The authors reported the characteristics and prognosis of gastric cancer in 920 patients who were treated in the authors’ hospital. The manuscript has been well designed and conducted. It revealed that for the elderly patient subset, in comparison with younger patient subsets, distant metastasis was less frequent, the efficacy of adjuvant chemotherapy was less effective, and the benefit of extended lymph-node dissection was unclear. A cancer-specific death rate was almost equal between the elderly subset and the younger subset, but overall mortality was higher in the former patient group. These data are very informative for the planning of strategy to treat the elderly patients with gastric cancer in China. The idea of the manuscript has potential instruction for clinicians.

**REFERENCES**

1. Endo S, Dousei T, Yoshikawa Y, Hatanaka N, Kamiike W, Nishijima J. Prognosis of gastric carcinoma patients aged 85 years or older who underwent surgery or who received best supportive care only. Int J Clin Oncol 2012 Oct 12; Epub ahead of print [PMID: 23065114 DOI: 10.1007/s10147-012-0482-9]

2. Endo S, Yoshikawa Y, Hatanaka N, Tominaga H, Shimizu Y, Hiraoka K, Nishitani A, Irei T, Nakashima S, Park MH, Takahashi H, Wakahara M, Kamiike W. Treatment for gastric carcinoma in the oldest old patients. Gastric Cancer 2011; 14: 139-143 [PMID: 21336856 DOI: 10.1007/s10120-011-0022-8]

3. Fujimoto S, Takahashi M, Ohkubo H, Mutou T, Kure M, Masaoka H, Kobayashi K. Comparative clinicopathologic features of early gastric cancer in young and older patients. Surgery 1994; 115: 516-520 [PMID: 8163544]
Liang YX et al. Age and gastric cancer

35 Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, Haller DG, Ajani JA, Gunderson LL, Jessup JM, Martenson JA. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001; 345: 725-730 [PMID: 11547741 DOI: 10.1056/NEJMoa010187]

36 Sakuramoto S, Sasako M, Yamaguchi T, Kinoshita T, Fujii M, Nashimoto A, Furukawa H, Nakajima T, Ohashi Y, Imamura H, Higashino M, Yamamura Y, Kurita A, Arai K. Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. N Engl J Med 2007; 357: 1810-1820 [PMID: 17978289 DOI: 10.1056/NEJMoa072252]

37 Wu Y, Wei ZW, He YL, Schwarz RE, Smith DD, Xia GK, Zhang CH. Efficacy of adjuvant XELOX and FOLFOX6 chemotherapy after D2 dissection for gastric cancer. World J Gastroenterol 2013; 19: 3309-3315 [PMID: 23745033 DOI: 10.3748/wjg.v19.i21.3309]

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