

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

Yue-Xiang Liang, Jing-Yu Deng, Han-Han Guo, Xue-Wei Ding, Xiao-Na Wang, Bao-Gui Wang, Li Zhang, Han Liang

Yue-Xiang Liang, Jing-Yu Deng, Xue-Wei Ding, Xiao-Na Wang, Bao-Gui Wang, Li Zhang, Han Liang, Department of Gastric Cancer, Tianjin Medical University Cancer Institute and Hospital, Key Laboratory of Cancer Prevention and Therapy, National Clinical Research Center of Cancer, Tianjin 300060, China
Han-Han Guo, Department of Cardiovascular Surgery, the First Hospital of Tianshui City, Tianshui 741000, Gansu Province, China

Author contributions: Liang YX, Liang H, Deng JY and Guo HH performed the majority of the study; Deng JY, Ding XW, Wang XN, Zhang L and Guo HH designed the study and analyzed data; Liang YX, Liang H, Wang BG and Guo HH wrote the manuscript; Deng JY, Ding XW, Wang BG and Wang XN revised the manuscript.

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Correspondence to: Han Liang, Professor, Department of Gastric Cancer, Tianjin Medical University Cancer Institute and Hospital, Key Laboratory of Cancer Prevention and Therapy, National Clinical Research Center of Cancer, Huanhuxi Road, Hexi District, Tianjin 300060, China. tjlianghan@sohu.com

Telephone: +86-22-23340123 Fax: +86-22-23340123

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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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Key words: Gastric carcinoma; Elderly patients; Prognosis; Lymphadenectomy; Chemotherapy

Core tip: Few studies have compared the characteristics and prognosis of gastric cancer among younger, middle-aged and elderly patients. Elderly patients have distinctive properties, and we have to treat them individually with particular care. We found that age ≥ 70 years was an independent prognostic factor for patients with gastric cancer after gastrectomy and these patients had distinctive characteristics of male predominance, larger tumor size, more histological differentiation, higher number 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.

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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 exists. 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. Negative resection margin was defined as microscopic complete resection, without residual cancer cells in the margin. Positive resection margin was defined as tumor cells < 1 mm from the cut edge or residual 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 χ^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, pT₄, N stage, M1, extent of lymphadenectomy, postoperative chemotherapy and age ≥ 70 years (hazard ratio: 1.487, $P = 0.003$) remained as independent prognostic factors for overall survival (OS). 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) (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 ≥ 70 years

Survival analysis of the elderly patients is shown in Table 4. Sex, tumor size, histology, extranodal metastasis, surgical margin status, pT₄, lymph node metastasis, M1 and type of gastrectomy were found to be prognostic factors in the univariate analysis, while only surgical margin status, pT₄, lymph node metastasis, M1 and sex were independent prognostic factors in the multivariate analysis. For patients aged ≥ 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 ≥ 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

Table 1 Case characteristics *n* (%)

Characteristics	Age (yr)			χ^2	P value
	< 50 (<i>n</i> = 166)	50-69 (<i>n</i> = 481)	≥ 70 (<i>n</i> = 273)		
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	5.035	0.007
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
pT ₁	4 (2.4)	12 (2.5)	6 (2.2)		
pT ₂	22 (13.3)	49 (10.2)	22 (8.1)		
pT ₃	5 (3.0)	30 (6.2)	17 (6.2)		
pT ₄	135 (81.3)	390 (81.1)	228 (83.5)		
Lymph node metastasis				5.325	0.503
pN ₀	62 (37.3)	170 (35.5)	87 (31.9)		
pN ₁	26 (15.7)	83 (17.3)	51 (18.7)		
pN ₂	32 (19.3)	108 (22.5)	73 (26.7)		
pN ₃	46 (27.7)	120 (24.9)	62 (22.7)		
Distant metastasis				9.251	0.010
M ₀	149 (89.8)	442 (91.9)	264 (96.7)		
M ₁	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 (46.2)	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
D ₂	89 (53.6)	222 (46.2)	91 (33.3)		
D ₁	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-

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

Characteristics	n (%)	5-yr OS	MST (mo)	Univariate analysis		Multivariate analysis	
				χ^2	P (log-rank)	Hazard ratio (95%CI)	P value
Gender				0.165	0.685		
Male	659 (71.6)	32.00%	26				
Female	261 (28.4)	33.70%	27				
Age (yr)				21.067	< 0.000		
< 50	166 (18.0)	38.00%	32			1 (ref)	
50-69	481 (52.3)	36.60%	28			1.107 (0.881, 1.391)	0.383
≥ 70	273 (29.7)	22.00%	20			1.487 (1.149, 1.924)	0.003
Tumor location				37.996	< 0.001		
Lower 1/3	372 (40.4)	40.10%	36			1 (ref)	
Middle 1/3	166 (18.0)	30.10%	18			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				51.052	< 0.001		
< 5 cm	375 (40.8)	45.10%	42			1 (ref)	
≥ 5 cm	545 (59.2)	23.90%	20			1.185 (0.994, 1.413)	0.058
Borrmann type				9.588	0.002		
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				13.994	< 0.001		
Differentiated	279 (30.3)	41.20%	34			1 (ref)	
Undifferentiated	641 (69.7)	28.70%	23			1.201 (0.996, 1.449)	0.055
Extranodal metastasis				61.626	< 0.001		
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				101.241	< 0.001		
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				67.084	< 0.001		
pT ₁	22 (2.4)	86.40%	69			1 (ref)	
pT ₂	93 (10.1)	61.30%	61			3.048 (0.937, 9.918)	0.064
pT ₃	52 (5.7)	46.20%	47			3.188 (0.965, 10.526)	0.057
pT ₄	753 (81.8)	26.40%	21			4.580 (1.431, 14.200)	0.010
Lymph node metastasis				243.605	< 0.001		
pN ₀	319 (34.7)	57.70%				1 (ref)	
pN ₁	160 (17.4)	31.90%	24			1.713 (1.327, 2.211)	< 0.001
pN ₂	213 (23.2)	23.50%	23			1.918 (1.514, 2.429)	< 0.001
pN ₃	228 (24.8)	6.10%	13			3.268 (2.572, 4.151)	< 0.001
Distant metastasis				89.428	< 0.001		
M ₀	855 (92.9)	34.70%	29			1 (ref)	
M ₁	65 (7.1)	3.10%	8			1.817 (1.339, 2.465)	< 0.001
Chemotherapy				17.080	< 0.001		
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				40.899	< 0.001		
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				4.060	0.044		
D ₂	402 (43.7)	36.60%	28			1 (ref)	
D ₁	518 (56.3)	29.30%	24			1.192 (1.005, 1.414)	0.043

Ref: Reference category; OS: Overall survival; MST: Median survival time.

proximately 1:1^[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^[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^[8,11,12], some researchers reported that cancer involving the upper third of the stomach was more common in elderly than in younger patients^[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 3 Survival analysis of younger, middle-aged and elderly patients stratified by tumor-node-metastasis stage

TNM	Younger (< 50 yr)			Middle-aged (50-69 yr)			Elderly (≥ 70 yr)			χ^2	P value
	n	5-yr OS	MST (mo)	n	5-yr OS	MST (mo)	n	5-yr OS	MST (mo)		
I	19	78.90%	68	43	81.40%	64	21	66.70%	66	1.200	0.594
II	45	53.30%	60	135	60.00%	61	72	33.30%	39	13.024	0.001
III	85	27.10%	24	264	22.30%	20	171	12.90%	16	11.874	0.003
IV	17	5.90%	10	39	2.60%	8	9	0.00%	6	2.909	0.233

MST: Median survival time; TNM: Tumor-node-metastasis; OS: Overall survival.

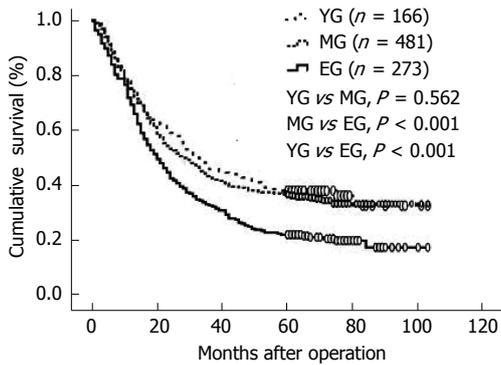


Figure 1 Overall survival curves for all patients grouped by age. Patients aged ≥ 70 years demonstrated a significantly lower 5-year OS rate than the younger and middle-aged patients (elderly vs middle-aged vs younger patients, 22.0% vs 36.6% vs 38.0%, respectively). EG: Elderly group; MG: Middle-aged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

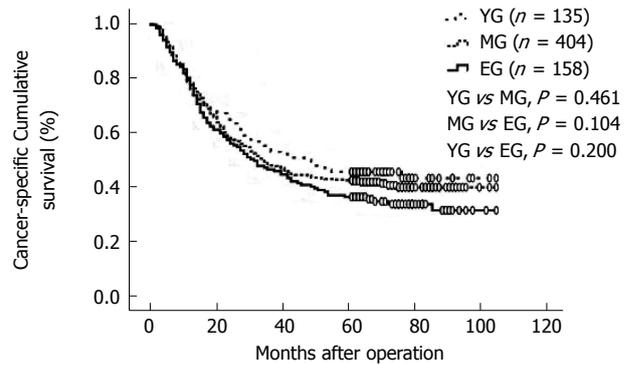


Figure 3 Cancer-specific survival of each age group. When deaths caused by factors other than gastric cancer were excluded, there were no significant differences in cancer-specific survival among the three age groups. EG: Elderly group; MG: Middle-aged group; YG: Younger group.

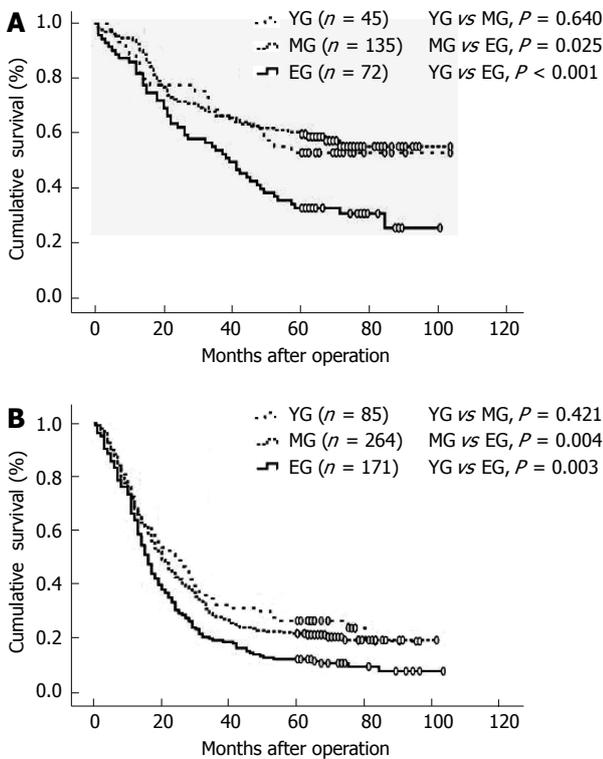


Figure 2 Overall survival curves for patients with tumor-node-metastasis II and III cancer. In the tumor-node-metastasis (TNM)-stratified analysis, the differences in overall survival (OS) were only observed in patients with TNM stage II and III cancer. A: Patients with II cancer; B: Patients with III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

elderly 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^[1,2]. 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]. How-

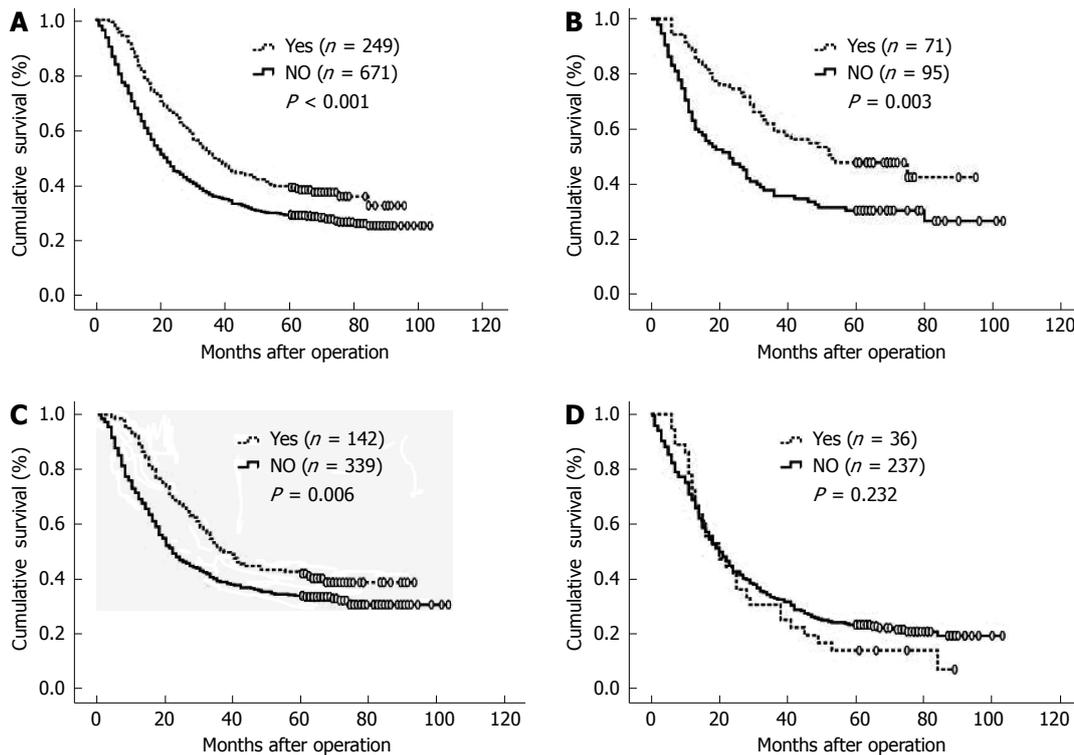


Figure 4 Overall survival curves for patients grouped by chemotherapy. In the age-stratified analysis, chemotherapy was a prognostic factor for the younger and middle-aged patients, but not for the elderly patients. A: All patients; B: Younger group; C: Middle-aged group; D: Elderly group.

ever, most studies confirmed the prognosis of elderly patients was poorer than that of younger and middle-aged patients^[9,16,17]. 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^[9,20]. 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, pT₄, 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 influ-

ence OS in elderly patients. In the present study, sex, surgical margin status, pT₄, 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

Table 4 Survival analysis of gastric cancer patients aged ≥ 70 years

Characteristics	n (%)	5-yr OS	MST (mo)	Univariate analysis		Multivariate analysis	
				χ^2	P (log-rank)	Hazard ratio (95%CI)	P value
Gender				4.009	0.045		
Female	58 (21.2)	29.30%	31			1 (ref)	
Male	215 (78.8)	20.00%	18			1.433 (1.013, 2.029)	0.042
Age (yr)				0.092	0.762		
< 75	164 (60.1)	23.20%	20				
≥ 75	109 (39.9)	20.20%	19				
Tumor location				6.055	0.109		
Lower 1/3	78 (28.6)	25.60%	22				
Middle 1/3	58 (21.2)	22.40%	15				
Upper 1/3	106 (38.8)	21.70%	22				
2/3 or more	31 (11.4)	12.90%	16				
Tumor size				8.715	0.003		
< 5 cm	87 (31.9)	32.20%	31			1 (ref)	
≥ 5 cm	186 (68.1)	17.20%	17			1.119 (0.816, 1.533)	0.485
Borrmann type				3.221	0.073		
I / II	95 (34.8)	27.40%	26				
III/IV	178 (65.2)	19.10%	18				
Histology				5.610	0.018		
Differentiated	116 (42.5)	28.40%	23			1 (ref)	
Undifferentiated	157 (57.5)	17.20%	18			1.272 (0.956, 1.693)	0.099
Extranodal metastasis				16.966	< 0.001		
Negative	223 (81.7)	24.70%	23			1 (ref)	
Positive	45 (18.3)	10.00%	11			1.248 (0.873, 1.784)	0.225
Surgical margin status				8.957	0.003		
Negative	241 (88.3)	24.10%	22			1 (ref)	
Positive	32 (11.7)	6.30%	12			1.583 (1.048, 2.391)	0.029
Depth of invasion				20.751	< 0.001		
pT ₁ -T ₃	45 (16.5)	51.10%	65			1 (ref)	
pT ₄	228 (83.5)	16.20%	17			1.773 (1.118, 2.811)	0.015
Lymph node metastasis				30.397	< 0.001		
pN ₀	87 (31.9)	40.20%	44			1 (ref)	
pT ₁ -N ₃	186 (68.1)	13.40%	16			1.658 (1.178, 2.334)	0.004
Distant metastasis				18.941	< 0.001		
M ₀	264 (96.7)	22.70%	21			2.332 (1.143, 4.756)	0.020
M ₁	9 (3.3)	0.00%	6				
Chemotherapy				0.508	0.476		
Yes	36 (13.2)	13.90%	20				
No	237 (86.8)	23.20%	20				
Type of gastrectomy				11.316	0.001		
Subtotal	214 (78.4)	24.80%	22			1 (ref)	
Total	59 (21.6)	11.90%	14			1.305 (0.936, 1.820)	0.117
Extent of lymphadenectomy				1.429	0.232		
D ₂	91 (33.3)	19.80%	17				
D ₁	182 (66.7)	23.10%	22				

Ref: Reference category; OS: Overall survival; MST: Median survival time.

Table 5 Comparison of survival rate for patients treated with chemotherapy or not stratified by age

Age (yr)	Chemotherapy						χ^2	P value
	Yes			No				
	n	5-yr OS	MST (mo)	n	5-yr OS	MST (mo)		
< 50	71	47.90%	53	95	30.50%	23	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.

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

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 > 70 years of age (3% for D1 and 13% for D2, $P = 0.36$)^[31]. 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)^[32]. In elderly patients, surgeons are usually reluctant to perform D2 resection to avoid major complications in the postoperative period^[18,33]. 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 ≥ 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^[34-36]. 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^[36]. 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^[37]. 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 ≥ 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 ≥ 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 ≥ 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 ≥ 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.

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