

The Impact of Intervention on Survival of Elderly Patients with Gastric Cancer at IV Stage: A SEER Population-Based Study.

Bo Cao

Chinese PLA General Hospital

Wenquan Liang

Chinese PLA General Hospital

Wang Zhang

Chinese PLA General Hospital

Chuang Wang

Chinese PLA General Hospital

Yajiao Shi

Chinese PLA General Hospital

Xin Zhou

Chinese PLA General Hospital

Bo Wei (✉ 18431143691@163.com)

Chinese PLA General Hospital <https://orcid.org/0000-0001-7386-2689>

Research article

Keywords: Gastric Cancer, Surgery, Chemotherapy, Survival, Elderly Patients

Posted Date: February 17th, 2020

DOI: <https://doi.org/10.21203/rs.2.23651/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background The selection of therapeutic regimens for elderly patients with gastric cancer (GC) has attracted much attention. However, few clinical trials have been conducted concerning the subpopulation of patients diagnosed with stage IV disease. In this study, cases from the Surveillance, Epidemiologic and End Results (SEER) database were collected to investigate the effects of surgery and chemotherapy (CT) on the survival benefit in elderly GC patients with stage IV disease.

Methods GC patients aged >65 years diagnosed with stage IV disease between 1973 and 2014 in the SEER database were included in the study pool based on strict inclusion and exclusion criteria. Univariate and multivariate analyses were employed to determine prognostic factors for overall survival (OS) and cancer-specific survival (CSS). Kaplan-Meier survival analysis was conducted to investigate the effects of different intervention methods on OS and CSS.

Results A total of 9,306 patients were selected from the SEER database. The results showed that patients who received both surgery and chemotherapy significantly obtained OS and CSS benefits ($P < 0.0001$). Compared with the no surgery and CT group, the CT alone group ($P < 0.0001$) and the surgery alone group ($P < 0.0001$) had prolonged survival time. Furthermore, age and grade stratifications served as important indicators for the selection of therapeutic regimens

Conclusions Surgery combined with CT outperformed monotherapy or no therapy strategies for elderly patients with stage IV disease.

Background

Gastric cancer (GC) is one of the most common malignancies worldwide. According to a new epidemiological investigation, the incidence and cancer-associated mortality of GC rank fourth and fifth, respectively[2]. GC has been recently identified as a kind of regional disease, whose incidence was found to be high in East Asia, South America and Eastern Europe but lower in America[20, 21, 24, 29]. Despite the tendency of GC patients to be diagnosed at a young age, the disease still mostly occurs in elderly patients, leading to poor prognosis[18]. Furthermore, due to their insensitivity to pain, deficiency of typical symptoms and intolerance of cachexia, elderly patients are usually severely affected by cancer and typically present distant metastasis at diagnosis. More attention should be paid to elderly patients with GC.

Traditional perspectives have shown high risks associated with positive interventions partly due to patient weakness and intolerance to treatment. However, with the development of evidence-based medicine, an increasing number of studies have demonstrated that positive interventions containing surgery or adjuvant chemotherapy (CT) will benefit survival for elderly GC patients. However, elderly patients who are suitable for intervention should meet some criteria, such as high nutrition level, proper physical functioning and some specific serum biomarkers[4, 11, 15, 16, 28]. Elderly patients with stage IV disease have always been neglected and designated as a treatment-invalid population. Little research

has focused on this subgroup to evaluate the effects of different therapeutic regimens on prolonging survival.

In this study, we employed the available data from the Surveillance, Epidemiologic and End Results (SEER) database to investigate surgical and therapeutic interventions in elderly GC patients diagnosed at stage IV to identify the best regimens for this subgroup.

Methods

Database

The SEER database is an authoritative resource of available cancer cases that can be utilized to investigate demographic, geographic and survival characteristics. The SEER research data include patient-associated clinical information, such as age, sex, race/ethnicity, marital status, insurance status and age/year of diagnosis, as well as large amounts of pathologic features, such as TNM classification, cancer grade, treatment method and survival data. The SEER*Stat software was used to search and download available data from the SEER database. The dataset in SEER was called "18 Regs Custom Data (with additional treatment fields), Nov 2016 Sub (1973–2014 varying)". Patients diagnosed with stage IV GC who were older than 65 years were selected for the initial patient pool. The age range in this study was based on that in previous studies that defined elderly patients[3, 28, 33]. Additionally, the behavioral type of tumors used for analysis was confined to "Malignant". To investigate the effect of different intervention methods on elderly GC patients with stage IV disease, information on relevant terms in this sample pool was extracted, which could be summarized as four aspects, including demographic information, clinicopathological features, therapeutic regimens and survival information. The collected data were further arranged and analyzed.

Variables

Variable information included sex, age, race, living region, marital status, median household income, insurance status, histologic type according to ICD-O-3, therapeutic records (surgery, CT and radiation), survival time and cause of death (COD) to site recode. The AJCC 6th edition TNM stage was collected for subsequent analysis rather than the AJCC 7th edition TNM stage because there was a lack of information on TNM stage based on the AJCC 7th edition in the patients diagnosed before 2010.

Demographic information was reorganized for convenience of analysis. The age at diagnosis was divided into five subgroups with intervals of 5 years, including "65–69", "70–74", "75–79", "80–84" and "≥85". Race was classified as "White, Black and Other (American Indian/AK Native, Asian/Pacific Islander)". The rural-urban living region was defined as three classified areas according the following groups: "Comp rural lt 2,500 urban pop, adjacent/not adjacent to a metro area" and "Fringe counties of metropolitan areas ge 1 million pop" were clustered together as "rural". "Counties in metropolitan areas of 250,000 to 1 million pop or lt 250 thousand pop" was classified as "county". "Urban pop of ge 20,000 adjacent/not adjacent to a metropolitan area" and "Urban pop of 2,500 to 19,999, adjacent/not adjacent

to a metro area” were classified as “urban”. Marital status included 6 items: “Married (including common law)” was classified as “married”. The not married cases were divided into two groups. One group included “Single (never married)”, “Divorced”, “Separated” and “Unmarried or Domestic Partner” cases. “Widowed” was grouped separately because it has been reported that widowed GC patients are at the highest risk of death compared with patients with other marital statuses[25]. Median household income was marked as “1–4” by quartile from lowest to highest for convenience of further investigations. For insurance status, the “Insured” and “Insured/No specifics” groups were clustered together as the “insured” group. The other cases were divided into “Medicaid”, “Uninsured” and “Unknown” groups.

Clinicopathological features included AJCC 6th TNM stage, histologic type and grade. For the T stage, “T2a”, “T2b” and “T2NOS” were all included in the “T2” group. Histologic type in the SEER database was determined according to ICD-O-3. The histologic type was defined as “Epithelial”, “Adenocarcinoma” or “Other”. The “Other” group included some rare kinds of GC, including squamous and complex epithelial types.

Therapeutic regimens were the main factors in this study. Patients who underwent surgery for primary tumor sites within the stomach or metastatic organs and tissues were all defined as having surgical intervention. Patients who received radiation were excluded from the study cohort to eliminate the effects of interventions unrelated to surgery and CT on survival time.

For survival information, the survival months of each patient and related COD information were rearranged for analysis of overall survival (OS) and cancer-specific survival (CSS), which were the primary outcomes in this study. The date of the last contact was regarded as the censored value for patients still alive.

Patient population

The selection criteria were key in this study. The inclusion criteria were as follows: a) patients diagnosed with GC pathologically; b) patients with an age of diagnosis over 65 years old; and c) patients diagnosed at stage IV. The exclusion criteria were as follows: a) patients with a lack of demographic information; b) patients with a lack of important clinical characteristics and treatment records; c) patients who were lost to follow-up; and d) patients who underwent radiotherapy. The pool of metastatic GC patients was utilized for further analysis.

Statistical methods

In general, demographic information, clinicopathological features, therapeutic regimens and survival information were summarized and rearranged for statistical comparisons. The differences in continuous variables were analyzed by Student’s t test. The differences in categorical variables were analyzed by the χ^2 test. This study aimed to investigate the potential risk factors of different therapeutic interventions. Kaplan-Meier curves and the log-rank test were employed to determine the effects of variables on OS and CCS. The independent prognostic factors were revised by the Cox proportional hazards model and used

to select the potential bias for the relationship between survival benefits and intervention methods. All statistical analyses were performed using SPSS 25.0. Statistical significance was set at a two-sided $P < 0.05$.

Results

Cohort description and patient characteristics

A total of 11,967 patients were initially selected from the SEER database in this study. After the exclusion of patients with a lack of information concerning basic demographic data, clinicopathological features and survival time, 10,968 patients remained for further investigation. To accurately analyze surgical and chemotherapeutic effects in GC, patients who had received radiotherapy were excluded to keep the intervention methods comparable. Ultimately, 9,306 patients were selected for statistical analysis. The selection procedure is shown in Fig. 1.

This pool was divided into four groups according to therapeutic regimens: 1) patients who received neither surgery nor CT ($n = 4,674$); 2) patients who received surgery alone ($n = 1,097$); 3) patients who received CT alone ($n = 2,969$); and 4) patients who received both surgery and CT ($n = 566$). The percentages of the groups were 50.23%, 11.79%, 31.90% and 6.08%, respectively. The clinical features of this cohort are presented in Table 1. There were significant differences between the four intervention groups regarding sex, age, ethnicity, marital status, median income, insurance status, T stage, N stage, histologic type and grade ($P < 0.05$).

Table 1

Characteristics of old patients of gastric cancer at \geq stage treated with four different intervention groups.

Clinicopathologic Characteristics	No surgery or CT	Surgery alone	CT alone	Surgery plus CT	P-value
Gender					< 0.001
Male	2767 (59.2%)	593 (54.1%)	2029 (68.3%)	330 (58.3%)	
Female	1907 (40.8%)	504 (45.9%)	940 (31.7%)	236 (41.7%)	
Age					< 0.001
65–69	754 (16.1%)	204 (18.6%)	949 (32.0%)	190 (33.6%)	
70–74	862 (18.4%)	238 (21.7%)	776 (26.1%)	164 (29.0%)	
75–79	1053 (22.5%)	256 (23.3%)	687 (23.1%)	121 (21.4%)	
80–84	1040 (22.3%)	241 (22.0%)	378 (12.7%)	65 (11.5%)	
\geq 85	965 (20.6%)	158 (14.4%)	179 (6.0%)	26 (4.6%)	
Ethnicity					< 0.001
White	3389 (72.5%)	764 (69.6%)	2258 (76.1%)	408 (72.1%)	
Black	653 (14.0%)	137 (12.5%)	362 (12.2%)	64 (11.3%)	
Other ¹	632 (13.5%)	196 (17.9%)	349 (11.8%)	94 (16.6%)	

CT chemotherapy

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	No surgery or CT	Surgery alone	CT alone	Surgery plus CT	P-value
Region					0.905
Urban	765 (16.4%)	174 (15.9%)	454 (15.3%)	85 (15.0%)	
County	3817 (81.7%)	903 (82.3%)	2454 (82.7%)	469 (82.9%)	
Rural	92 (2.0%)	20 (1.8%)	61 (2.1%)	12 (2.1%)	
Marital status					< 0.001
Married	2298 (49.2%)	622 (56.7%)	1985 (66.9%)	373 (65.9%)	
Single or divorced ²	945 (20.2%)	166 (15.1%)	510 (17.2%)	96 (17.0%)	
Widowed	1431 (30.6%)	309 (28.2%)	474 (16.0%)	97 (17.1%)	
Median income					0.046
1(lowest)	1193 (25.5%)	271 (24.7%)	723 (24.4%)	138 (24.4%)	
2	1266 (27.1%)	297 (27.1%)	714 (24.0%)	140 (24.7%)	
3	1144 (24.5%)	267 (24.3%)	761 (25.6%)	150 (26.5%)	
4(highest)	1071 (22.9%)	262 (23.9%)	771 (26.0%)	138 (24.4%)	
Insurance					< 0.001
Insured ³	2719 (58.2%)	531 (48.4%)	2066 (69.6%)	345 (61.0%)	

CT chemotherapy
1 American Indian/AK Native, Asian/Pacific Islander
2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner
3 Insured, and Insured/No specifics
4 T2a, T2b and T2NOS
5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	No surgery or CT	Surgery alone	CT alone	Surgery plus CT	P-value
Medicaid	533 (11.4%)	129 (11.8%)	246 (8.3%)	52 (9.2%)	
Uninsured	54 (1.2%)	7 (0.6%)	25 (0.8%)	11 (1.9%)	
Unknown	1368 (29.3%)	430 (39.2%)	632 (21.3%)	158 (27.9%)	
T stage					< 0.001
T0	22 (0.5%)	4 (0.4%)	14 (0.5%)	4 (0.7%)	
T1	930 (19.9%)	70 (6.4%)	612 (20.6%)	52 (9.2%)	
T2 ⁴	436 (9.3%)	333 (30.4%)	427 (14.4%)	165 (29.2%)	
T3	132 (2.8%)	296 (27.0%)	122 (4.1%)	143 (25.3%)	
T4	803 (17.2%)	287 (26.2%)	435 (14.7%)	130 (23.0%)	
Tx	2351 (50.3%)	107 (9.8%)	1359 (45.8%)	72 (12.7%)	
N stage					< 0.001
N0	1839 (39.3%)	245 (22.3%)	1069 (36.0%)	134 (23.7%)	
N1	1132 (24.2%)	394 (35.9%)	1037 (34.9%)	223 (39.4%)	
N2	56 (1.2%)	225 (20.5%)	80 (2.7%)	106 (18.7%)	

CT chemotherapy
1 American Indian/AK Native, Asian/Pacific Islander
2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner
3 Insured, and Insured/No specifics
4 T2a, T2b and T2NOS
5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	No surgery or CT	Surgery alone	CT alone	Surgery plus CT	P-value
N3	20 (0.4%)	114 (10.4%)	37 (1.2%)	52 (9.2%)	
Nx	1627 (34.8%)	119 (10.8%)	746 (25.1%)	51 (9.0%)	
Histologic type					< 0.001
Epithelial	372 (8.0%)	30 (2.7%)	137 (4.6%)	11 (1.9%)	
Adenocarcinoma	3434 (73.5%)	785 (71.6%)	2255 (76.0%)	401 (70.8%)	
Other ⁵	868 (18.6%)	282 (25.7%)	577 (19.4%)	154 (27.2%)	
Grade					< 0.001
Well	104 (2.2%)	25 (2.3%)	67 (2.3%)	8 (1.4%)	
Moderately	864 (18.5%)	199 (18.1%)	610 (20.5%)	123 (21.7%)	
Poorly	2340 (50.1%)	722 (65.8%)	1584 (53.4%)	345 (61.0%)	
Undifferentiated	79 (1.7%)	29 (2.6%)	49 (1.7%)	11 (1.9%)	
Unknown	1287 (27.5%)	122 (11.1%)	659 (22.2%)	79 (14.0%)	
CT chemotherapy					
1 American Indian/AK Native, Asian/Pacific Islander					
2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner					
3 Insured, and Insured/No specifics					
4 T2a, T2b and T2NOS					
5 Squamous and complex epithelial gastric cancer					

Univariate and multivariate analysis of OS and CSS prognostic factors

To screen prognostic factors for OS and CSS, univariate analysis was first conducted. The results showed that age, race, marital status, insurance status, median income, N stage, histologic type and therapeutic methods were statistically associated with the OS of patients. Additionally, a race of American Indian/AK

Native, Asian/Pacific Islander, the county region, being uninsured, T2 stage, poorly differentiated status and unknown grade were also correlated with OS ($P < 0.05$, Table 2). In addition, sex, age, black race, being married, unknown insurance status, N stage, histologic type, grade, and therapeutic method were significantly associated with CSS (Table 3). Furthermore, multivariate analysis was employed to screen out independent prognostic factors of OS and CSS. The modified model indicated that age, American Indian/AK Native, Asian/Pacific Islander race, being single (never married), being divorced, being separated and being unmarried or being with a domestic partner, the second lowest income bracket, therapeutic method, insurance status, T2 stage, and grade were independent prognostic factors for OS. The independent prognostic factors for CSS were similar to those for OS, including age, black race, the second lowest income bracket, unknown insurance status, N1 stage, grade and therapeutic method.

Table 2

Univariate and multivariate analysis of OS for old patients at \geq stage with gastric cancer.

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
Gender					
Male	5719 (61.5%)	Reference		Reference	
Female	3587 (38.5%)	1.03 (0.98, 1.07)	0.2170	0.91 (0.87, 0.96)	0.0002
Age					
65–69	2097 (22.5%)	Reference		Reference	
70–74	2040 (21.9%)	1.13 (1.06, 1.20)	0.0002	1.09 (1.02, 1.16)	0.0086
75–79	2117 (22.7%)	1.27 (1.20, 1.36)	< 0.0001	1.14 (1.07, 1.21)	< 0.0001
80–84	1724 (18.5%)	1.44 (1.35, 1.54)	< 0.0001	1.14 (1.06, 1.22)	0.0002
\geq 85	1328 (14.3%)	1.79 (1.67, 1.93)	< 0.0001	1.27 (1.18, 1.38)	< 0.0001
Ethnicity					
White	6819 (73.3%)	Reference		Reference	
Black	1216 (13.1%)	1.06 (0.99, 1.12)	0.0932	1.04 (0.97, 1.11)	0.2450
Other ¹	1271 (13.7%)	0.92 (0.87, 0.98)	0.0128	0.91 (0.86, 0.98)	0.0066
Region					

CT chemotherapy; OS overall survival.

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
Urban	1478 (15.9%)	Reference		Reference	
County	7643 (82.1%)	0.93 (0.88, 0.99)	0.0171	0.98 (0.92, 1.05)	0.5474
Rural	185 (2.0%)	0.92 (0.78, 1.08)	0.3223	0.97 (0.83, 1.14)	0.7207
Marital status					
Married	5278 (56.7%)	Reference		Reference	
Single or divorced ²	1717 (18.5%)	1.14 (1.08, 1.21)	< 0.0001	1.07 (1.00, 1.13)	0.0360
Widowed	2311 (24.8%)	1.27 (1.21, 1.34)	< 0.0001	1.03 (0.97, 1.09)	0.3237
Median income					
1(lowest)	2325 (25.0%)	Reference		Reference	
2	2417 (26.0%)	0.92 (0.87, 0.98)	0.0065	0.88 (0.83, 0.95)	0.0003
3	2322 (25.0%)	0.96 (0.90, 1.01)	0.1307	0.97 (0.91, 1.03)	0.3511
4(highest)	2242 (24.1%)	0.91 (0.85, 0.96)	0.0016	0.94 (0.88, 1.01)	0.1145
Insurance					
Insured ³	5661 (60.8%)	Reference		Reference	

CT chemotherapy; OS overall survival.

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
Medicaid	960 (10.3%)	1.03 (0.95, 1.10)	0.4990	0.93 (0.86, 1.00)	0.0415
Uninsured	97 (1.0%)	0.80 (0.63, 1.01)	0.0655	0.78 (0.61, 0.99)	0.0373
Unknown	2588 (27.8%)	1.14 (1.08, 1.19)	< 0.0001	1.04 (0.99, 1.09)	0.1116
T stage					
T0	44 (0.5%)	Reference		Reference	
T1	1664 (17.9%)	0.85 (0.62, 1.17)	0.3203	0.80 (0.58, 1.09)	0.1620
T2 ⁴	1361 (14.6%)	0.66 (0.48, 0.90)	0.0086	0.72 (0.52, 0.99)	0.0427
T3	693 (7.4%)	0.67 (0.48, 0.92)	0.0125	0.77 (0.56, 1.07)	0.1153
T4	1655 (17.8%)	0.92 (0.67, 1.26)	0.6119	0.89 (0.65, 1.22)	0.4662
Tx	3889 (41.8%)	0.95 (0.70, 1.30)	0.7652	0.84 (0.62, 1.16)	0.2917
N stage					
N0	3287 (35.3%)	Reference		Reference	
N1	2786 (29.9%)	0.84 (0.80, 0.89)	< 0.0001	0.95 (0.90, 1.01)	0.0988
N2	467 (5.0%)	0.71 (0.64, 0.78)	< 0.0001	0.96 (0.86, 1.07)	0.4568

CT chemotherapy; OS overall survival.

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
N3	223 (2.4%)	0.73 (0.64, 0.84)	< 0.0001	0.99 (0.85, 1.15)	0.8989
Nx	2543 (27.3%)	1.17 (1.11, 1.24)	< 0.0001	1.04 (0.99, 1.11)	0.1335
Histologic type					
Epithelial	550 (5.9%)	Reference		Reference	
Adenocarcinoma	6875 (73.9%)	0.75 (0.68, 0.82)	< 0.0001	0.95 (0.87, 1.05)	0.3221
Other ⁵	1881 (20.2%)	0.78 (0.71, 0.86)	< 0.0001	1.01 (0.91, 1.12)	0.8605
Grade					
Well	204 (2.2%)	Reference		Reference	
Moderately	1796 (19.3%)	1.08 (0.93, 1.26)	0.3234	1.23 (1.05, 1.44)	0.0093
Poorly	4991 (53.6%)	1.26 (1.09, 1.47)	0.0023	1.51 (1.30, 1.76)	< 0.0001
Undifferentiated	168 (1.8%)	1.40 (1.13, 1.74)	0.0022	1.65 (1.33, 2.05)	< 0.0001
Unknown	2147 (23.1%)	1.42 (1.22, 1.66)	< 0.0001	1.44 (1.23, 1.68)	< 0.0001
Therapeutic methods					
No surgery or CT	4674 (50.2%)	Reference		Reference	
Surgery alone	1097 (11.8%)	0.50 (0.47, 0.54)	< 0.0001	0.55 (0.50, 0.59)	< 0.0001

CT chemotherapy; OS overall survival.

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
CT alone	2969 (31.9%)	0.36 (0.34, 0.38)	< 0.0001	0.37 (0.35, 0.39)	< 0.0001
Surgery plus CT	566 (6.1%)	0.25 (0.23, 0.28)	< 0.0001	0.28 (0.25, 0.31)	< 0.0001
CT chemotherapy; OS overall survival.					
1 American Indian/AK Native, Asian/Pacific Islander					
2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner					
3 Insured, and Insured/No specifics					
4 T2a, T2b and T2NOS					
5 Squamous and complex epithelial gastric cancer					

Table 3

Univariate and multivariate analysis of CSS for old patients at \geq stage with gastric cancer.

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
Gender					
Male	5719 (61.5%)	Reference		Reference	
Female	3587 (38.5%)	1.12 (1.07, 1.18)	< 0.0001	0.99 (0.94, 1.05)	0.7952
Age					
65–69	2097 (22.5%)	Reference		Reference	
70–74	2040 (21.9%)	1.15 (1.07, 1.24)	0.0001	1.11 (1.03, 1.19)	0.0056
75–79	2117 (22.7%)	1.30 (1.21, 1.40)	< 0.0001	1.16 (1.07, 1.25)	0.0001
80–84	1724 (18.5%)	1.48 (1.37, 1.59)	< 0.0001	1.17 (1.08, 1.26)	0.0001
\geq 85	1328 (14.3%)	1.87 (1.72, 2.03)	< 0.0001	1.32 (1.21, 1.44)	< 0.0001
Ethnicity					
White	6819 (73.3%)	Reference		Reference	
Black	1216 (13.1%)	1.13 (1.05, 1.21)	0.0008	1.13 (1.05, 1.22)	0.0013
Other ¹	1271 (13.7%)	1.05 (0.98, 1.13)	0.1491	1.03 (0.96, 1.10)	0.4667
Region					

CT chemotherapy; CSS cancer-specific survival.

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
Urban	1478 (15.9%)	Reference		Reference	
County	7643 (82.1%)	0.96 (0.90, 1.03)	0.2669	0.99 (0.92, 1.07)	0.8013
Rural	185 (2.0%)	0.92 (0.77, 1.11)	0.4015	0.98 (0.81, 1.18)	0.8390
Marital status					
Married	5278 (56.7%)	Reference		Reference	
Single or divorced ²	1717 (18.5%)	1.11 (1.04, 1.18)	0.0020	1.01 (0.94, 1.08)	0.7566
Widowed	2311 (24.8%)	1.31 (1.24, 1.39)	< 0.0001	1.01 (0.95, 1.08)	0.7529
Median income					
1(lowest)	2325 (25.0%)	Reference		Reference	
2	2417 (26.0%)	0.95 (0.89, 1.02)	0.1711	0.90 (0.84, 0.97)	0.0089
3	2322 (25.0%)	0.97 (0.90, 1.04)	0.3368	0.98 (0.91, 1.06)	0.5899
4(highest)	2242 (24.1%)	0.94 (0.88, 1.01)	0.0705	0.96 (0.88, 1.04)	0.3002
Insurance					
Insured ³	5661 (60.8%)	Reference		Reference	

CT chemotherapy; CSS cancer-specific survival.

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
Medicaid	960 (10.3%)	1.05 (0.97, 1.14)	0.2052	0.93 (0.86, 1.01)	0.0913
Uninsured	97 (1.0%)	0.87 (0.67, 1.13)	0.3115	0.87 (0.67, 1.12)	0.2807
Unknown	2588 (27.8%)	1.19 (1.13, 1.26)	< 0.0001	1.07 (1.02, 1.14)	0.0108
T stage					
T0	44 (0.5%)	Reference		Reference	
T1	1664 (17.9%)	1.10 (0.73, 1.67)	0.6378	1.05 (0.69, 1.59)	0.8099
T2 ⁴	1361 (14.6%)	0.92 (0.61, 1.39)	0.6856	1.03 (0.68, 1.56)	0.8847
T3	693 (7.4%)	0.94 (0.62, 1.43)	0.7715	1.10 (0.72, 1.68)	0.6490
T4	1655 (17.8%)	1.32 (0.87, 1.99)	0.1919	1.27 (0.84, 1.93)	0.2512
Tx	3889 (41.8%)	1.27 (0.84, 1.91)	0.2582	1.13 (0.75, 1.71)	0.5540
N stage					
N0	3287 (35.3%)	Reference		Reference	
N1	2786 (29.9%)	0.82 (0.77, 0.87)	< 0.001	0.92 (0.86, 0.98)	0.0069
N2	467 (5.0%)	0.71 (0.63, 0.80)	< 0.001	0.91 (0.80, 1.04)	0.1536

CT chemotherapy; CSS cancer-specific survival.

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
N3	223 (2.4%)	0.76 (0.65, 0.89)	< 0.001	0.96 (0.82, 1.14)	0.6534
Nx	2543 (27.3%)	1.18 (1.11, 1.25)	< 0.001	1.05 (0.99, 1.12)	0.1255
Histologic type					
Epithelial	550 (5.9%)	Reference		Reference	
Adenocarcinoma	6875 (73.9%)	0.75 (0.67, 0.83)	< 0.0001	0.97 (0.87, 1.07)	0.5200
Other ⁵	1881 (20.2%)	0.83 (0.74, 0.93)	0.0010	1.06 (0.95, 1.19)	0.2833
Grade					
Well	204 (2.2%)	Reference		Reference	
Moderately	1796 (19.3%)	1.09 (0.91, 1.31)	0.3522	1.24 (1.03, 1.49)	0.0218
Poorly	4991 (53.6%)	1.37 (1.15, 1.63)	0.0005	1.60 (1.34, 1.91)	< 0.0001
Undifferentiated	168 (1.8%)	1.50 (1.17, 1.92)	0.0013	1.75 (1.37, 2.25)	< 0.0001
Unknown	2147 (23.1%)	1.50 (1.25, 1.79)	< 0.0001	1.49 (1.24, 1.79)	< 0.0001
Therapeutic methods					
No surgery or CT	4674 (50.2%)	Reference		Reference	
Surgery alone	1097 (11.8%)	0.51 (0.47, 0.55)	< 0.0001	0.53 (0.49, 0.58)	< 0.0001

CT chemotherapy; CSS cancer-specific survival.

1 American Indian/AK Native, Asian/Pacific Islander

2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner

3 Insured, and Insured/No specifics

4 T2a, T2b and T2NOS

5 Squamous and complex epithelial gastric cancer

Clinicopathologic Characteristics	Total (n)	Univariate	P-value	Multivariate	P-value
		HR		HR	
CT alone	2969 (31.9%)	0.34 (0.32, 0.36)	< 0.0001	0.36 (0.34, 0.39)	0.0001
Surgery plus CT	566 (6.1%)	0.27 (0.24, 0.30)	< 0.0001	0.29 (0.26, 0.33)	< 0.0001
CT chemotherapy; CSS cancer-specific survival.					
1 American Indian/AK Native, Asian/Pacific Islander					
2 Single (never married), Divorced, Separated and Unmarried or Domestic Partner					
3 Insured, and Insured/No specifics					
4 T2a, T2b and T2NOS					
5 Squamous and complex epithelial gastric cancer					

Survival outcomes of different therapeutic methods

Kaplan-Meier survival analysis was employed to compare survival time and accumulative hazards of OS and CSS between the four intervention regimens (Fig. 2). The results showed that the patients who received surgery plus CT obtained the best survival benefit [(HR of OS = 0.28, 95% CI = 0.25–0.31, $P < 0.0001$) (HR of CSS = 0.29, 95% CI = 0.26–0.33, $P < 0.0001$)], while patients who received neither method obtained the worst survival benefit. The survival of the CT alone group [(HR of OS = 0.37, 95% CI = 0.35–0.39, $P < 0.0001$) (HR of CSS = 0.36, 95% CI = 0.34–0.39, $P = 0.0001$)] was better than that of the surgery alone group [(HR of OS = 0.55, 95% CI = 0.50–0.59, $P < 0.0001$) (HR of CSS = 0.53, 95% CI = 0.49–0.58, $P < 0.0001$)].

Stratified analysis for survival of elderly patients with stage IV disease

According to the univariate and multivariate analyses of OS and CSS, age and grade were important prognostic factors with gradient changes in terms of survival. Therefore, stratified analysis was conducted to investigate the effects of age and grade on OS (Figs. 3, 4) and CSS (Figs. 5, 6) by dividing the patients into four therapeutic groups to explore suitable subpopulations for surgery and CT. The hazards of OS and CSS after age stratification were similar to those identified in the unstratified results (Additional file 1, 2). The Cox proportional hazard model showed that the OS and CSS gaps between the CT alone group and surgery alone group were increasingly narrowed with increasing age. When patients were stratified according to the “Undifferentiated” grade parameter (Additional file 3, 4), the best OS and CSS values were shown in the surgery alone group [(HR of OS = 0.32, 95% CI = 0.16–0.63, $P = 0.0009$) (HR of CSS = 0.26, 95% CI = 0.12–0.56, $P = 0.0006$)]. Notably, the best CSS benefit with surgery plus CT treatment was shown in the well-differentiated group [(HR of CSS = 0.14, 95% CI = 0.04–0.56, $P = 0.0049$)],

which decreased the CSS hazard ratio by at least 10% in comparison with the hazard ratios seen in the other stratified group.

Discussion

The selection of therapeutic regimens for elderly GC patients has been a hot topic in clinical practice. Compared with younger GC patients, elderly individuals mostly have poor prognosis and short survival[18]. Traditional thoughts have suggested that surgery and CT are not suitable for elderly patients given considerations of quality of life and the cost-benefit ratio. However, recent studies have shown that appropriate interventions for elderly patients can significantly improve survival[3, 11, 15]. Clarification of the significance of positive interventions in elderly patients seems necessary.

This study focused on the relationship between survival and therapeutic regimens in a specific subgroup of elderly GC patients, those with cancer metastasis. Information on elderly GC patients with stage IV disease from the SEER database was extracted, including demographic information, clinicopathological features, therapeutic regimens and survival information. The cohort consisted of 9,603 patients after a strict selection procedure. OS and CSS were the primary outcomes. Modification of the multivariate analysis showed that age, the second lowest income bracket, grade and therapeutic method were independent prognostic factors.

Surgical intervention for elderly GC patients has always been controversial. There are two purposes of surgical intervention for elderly patients with stage IV disease: prolonging survival time and alleviating cancer-associated symptoms. Although Katai et al[10] reported nonideal short-term survival after surgery in elderly patients ten years ago, some recent studies have demonstrated that the postoperative morbidity and mortality in elderly patients are comparable with those in younger patients[19, 22], which may be attributable to advances in nutritional support, anesthesia, surgical instruments and skills. The benefits of surgery plus CT for the survival of GC patients with stage IV disease were also clearly identified[12, 26, 27, 32]. The postoperative complication rate was not different between elderly populations of different ages, which suggested that the benefits of surgical intervention would not decrease with age. CT has been recommended as the main method for treating stage IV GC[1]. Its efficacy for metastatic GC has been proven by many clinical trials. Increasingly more effective drugs and regimens have also been refined[6, 7, 9, 31].

In this study, the therapeutic methods were the main factors for patient survival. Patients who underwent treatment with both surgery and CT acquired the best OS and CSS values. Conversely, the no surgery or CT group had the shortest OS and CSS values. Surgery and CT decreased the risks of OS and CSS by 72% and 71%, respectively. Only surgery or CT obtained survival benefits compared with no treatment. The advantages of Surgery plus CT for survival outcomes were consistent with those identified in previous studies[8, 23]. Furthermore, the OS and CSS values associated with CT alone were significantly better than those associated with surgery alone. This suggests that CT is a better choice than surgery for

elderly patients with stage IV disease who cannot receive both, which may be due to the noninvasive methods and relief of stress associated with CT.

However, in the cohort of this study, only 6.1% patients received surgery and CT. The percentages of patients who received surgery or CT alone were 11.8% and 31.9%, respectively. Nearly half of the patients received neither surgery nor CT. Moreover, the number of patients who received surgery decreased with increasing age, which was consistent with a previous study[22]. Few elderly patients choose positive interventions, especially combined surgical and chemotherapeutic interventions, due to their physical status and the risk-benefit ratio. Pre-existing views of patients and their families about the side effects of surgery and CT might be another reason that positive intervention was not chosen.

To classify the most appropriate subpopulation who can benefit from positive intervention, a stratified analysis according to age and grade was conducted. For age, the effects of the four therapeutic methods on OS and CSS were similar to those seen in the unstratified results. Patients who underwent surgery and CT achieved the best survival, while the no treatment group had the worst survival. With increasing age, patients received less survival benefit from both or single intervention methods, as previous studies have reported[17, 30]. Moreover, an increase in age also narrowed the survival gap between the surgery alone and CT alone groups. The OS and CSS hazards associated with surgery alone generally declined, while those associated with CT alone increased. There are two possible reasons for these results. 1) The remaining natural life span decreases with increasing age, which impairs the original capabilities of these interventions. The survival time was more subject to innate life influences in elderly patients than in younger patients; 2) adverse effects of CT might be more severe in the oldest elderly patients.

After stratification by cancer grade, the effects for the intervention methods were similar. Loss of cancer cell differentiation can decrease the survival rate. Notably, the well-differentiated groups achieved the best survival through surgery alone or surgery plus CT treatment. Surgery and the combination of surgery and CT resulted in less survival benefit from well to poorly differentiated GC, whereas CT alone had more effects on the dedifferentiation tendency of cells. The trend was opposite for the “undifferentiated” group. Patients with undifferentiated GC can be recommended for surgical treatment if only surgery or CT is used. This suggests that grade serves as an important therapeutic indicator for elderly patients with stage IV disease. Comprehensive regimens should be strictly established in consideration of GC grades.

The SEER database is an authoritative database, whose cancer incidence data from population-based cancer registries covers approximately 34.6% of the U.S. population. Some published articles from SEER data have investigated the relationships of elderly GC patients and therapeutic efficacy[5, 13, 14, 33]. This study first focused on the evaluation of the effects of surgical and chemotherapeutic methods in elderly GC patients with stage IV disease from the SEER database. The subpopulation of GC patients had features similar to those of young patients or all elderly patients. However, this study also revealed unique characteristics of elderly patients with stage IV disease. First, for the general survival and stratified analysis, the results were concluded as “surgery plus CT > CT alone > surgery alone > no surgery or CT”. Second, the efficacy of CT alone was significantly superior to that of surgery alone, but the survival gap

narrowed and even faded away with increasing age. Third, the GC grade was an important indicator of the success of the intervention methods and thus could be used for the prediction of therapeutic efficacy and the selection of the most appropriate regimens. Undoubtedly, shortcomings existed in the study: elderly patients who received surgery could have had better physical status and health-care conditions than those who did not receive surgery, which might lead to selection bias in the survival outcomes; another limitation was the lack of detailed information in the recorded data, such as surgical methods and CT drugs. This missing information could have caused potential biases in the final results.

Conclusions

Our findings show that the surgery + CT regimen is the most effective method in terms of survival benefit among elderly GC patients with stage IV disease. CT alone and surgery alone can also improve survival to some extent compared with no treatment. Age and cancer grade serve as important indicators for the selection of intervention methods. Future comparative studies with more detailed analysis and strict exclusion of bias factors are needed to further identify appropriate regimens for elderly GC patients with stage IV disease.

Abbreviations

Words	Abbreviations
Chemotherapy	CT
Gastric Cancer	GC
Surveillance, Epidemiologic and End Results	SEER
Overall Survival	OS
Cancer-specific Survival	CSS
Cause of Death	COD
Hazard Ratio	HR
Confidence Interval	CI

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are available in the SEER database repository, <https://seer.cancer.gov/>.

Competing interests

The authors declare that they have no competing interests.

Funding

1. National Natural Science Foundation of China, 81773135;
2. Beijing Science and Technology Commission Bio-Medicine and Bio-Science

Innovation Research Major Subject, Z171100000417023.

Authors' contributions

BC was responsible for acquisition of data, further analysis and mainly drafting the manuscript. WL and WZ were responsible for design of the work and revising the manuscript critically. CW was responsible for curation of the data and revising the manuscript critically. YS and XZ were responsible for interpretation of data and partly drafting the work. BW was responsible for the conception of the work and revising it critically. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

References

1. Ajani JA, Bentrem DJ, Besh S, D'Amico TA, Das P, Denlinger C, et al. Gastric cancer, version 2.2013: featured updates to the NCCN Guidelines. *J Natl Compr Canc Netw* 2013;11:531-546.

2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394-424.
3. Chang SH, Kim SN, Choi HJ, Park M, Kim RB, Go SI, et al. Adjuvant Chemotherapy for Advanced Gastric Cancer in Elderly and Non-elderly Patients: Meta-Analysis of Randomized Controlled Trials. *Cancer Res Treat* 2017;49:263-273.
4. Choo JW, Ju Y, Lim H, Youn SH, Soh JS, Park JW, et al. Is it beneficial to perform surgical resection in elderly patients more than 80 years old with advanced gastric cancer? *Scand J Gastroenterol* 2017;52:1057-1064.
5. Dudeja V, Habermann EB, Zhong W, Tuttle TM, Vickers SM, Jensen EH, et al. Guideline Recommended Gastric Cancer Care in the Elderly: Insights into the Applicability of Cancer Trials to Real World. *Ann Surg Oncol* 2010;18:26-33.
6. Ford HER, Marshall A, Bridgewater JA, Janowitz T, Coxon FY, Wadsley J, et al. Docetaxel versus active symptom control for refractory oesophagogastric adenocarcinoma (COUGAR-02): an open-label, phase 3 randomised controlled trial. *The Lancet Oncology* 2014;15:78-86.
7. Fuchs CS, Tomasek J, Yong CJ, Dumitru F, Passalacqua R, Goswami C, et al. Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): an international, randomised, multicentre, placebo-controlled, phase 3 trial. *The Lancet* 2014;383:31-39.
8. Fukuchi M, Mochiki E, Ishiguro T, Kumagai Y, Ishibashi K, Ishida H. Prognostic Significance of Conversion Surgery Following First- or Second-line Chemotherapy for Unresectable Gastric Cancer. *Anticancer Res* 2018;38:6473-6478.
9. Kang JH, Lee SI, Lim DH, Park KW, Oh SY, Kwon HC, et al. Salvage chemotherapy for pretreated gastric cancer: a randomized phase III trial comparing chemotherapy plus best supportive care with best supportive care alone. *J Clin Oncol* 2012;30:1513-1518.
10. Katai H, Sasako M, Sano T, Maruyama K. The outcome of surgical treatment for gastric carcinoma in the elderly. *Jpn J Clin Oncol* 1998;28:112-115.
11. Li Y, Tan B, Fan L, Zhao Q, Tan M, Wang D, et al. Clinicopathologic Characteristics of Elderly with Gastric Cancer, and the Risk Factors of Postoperative Complications. *J Invest Surg* 2017;30:394-400.
12. Li Z, Fan B, Shan F, Tang L, Bu Z, Wu A, et al. Gastrectomy in comprehensive treatment of advanced gastric cancer with synchronous liver metastasis: a prospectively comparative study. *World J Surg Oncol* 2015;13:212.
13. Liu KT, Wan JF, Yu GH, Bei YP, Chen X, Lu MZ. The recommended treatment strategy for locally advanced gastric cancer in elderly patients aged 75 years and older: a Surveillance, Epidemiology, and End Results database analysis. *J Cancer Res Clin Oncol* 2017;143:313-320.
14. Liu N, Molena D, Stem M, Blackford AL, Sewell DB, Lidor AO. Underutilization of Treatment for Regional Gastric Cancer Among the Elderly in the USA. *J Gastrointest Surg* 2018;22:955-963.

15. Ma X, Ren D, Kan J, Zheng F, Zhang S, Zhang Y, et al. Clinicopathological Characteristics and Prognoses of Elderly Gastric Cancer Patients after R0 Resection: A Multicenter Study in China. *J Environ Pathol Toxicol Oncol* 2018;37:81-91.
16. Mikami K, Hirano K, Futami K, Maekawa T. Gastrectomy with limited surgery for elderly patients with gastric cancer. *Asian J Surg* 2018;41:65-72.
17. Nelen SD, van Putten M, Lemmens V, Bosscha K, de Wilt JHW, Verhoeven RHA. Effect of age on rates of palliative surgery and chemotherapy use in patients with locally advanced or metastatic gastric cancer. *Br J Surg* 2017;104:1837-1846.
18. Nelen SD, Verhoeven RHA, Lemmens V, de Wilt JHW, Bosscha K. Increasing survival gap between young and elderly gastric cancer patients. *Gastric Cancer* 2017;20:919-928.
19. Orsenigo E, Tomajer V, Palo SD, Carlucci M, Vignali A, Tamburini A, et al. Impact of age on postoperative outcomes in 1118 gastric cancer patients undergoing surgical treatment. *Gastric Cancer* 2007;10:39-44.
20. Pokala SK, Zhang C, Chen Z, Gamboa AM, Cristofaro SL, Keilin SA, et al. Lymph node metastasis in early gastric adenocarcinoma in the United States of America. *Endoscopy* 2018;50:479-486.
21. Rahman R, Asombang AW, Ibdah JA. Characteristics of gastric cancer in Asia. *World J Gastroenterol* 2014;20:4483-4490.
22. Sakurai K, Muguruma K, Nagahara H, Kimura K, Toyokawa T, Amano R, et al. The outcome of surgical treatment for elderly patients with gastric carcinoma. *J Surg Oncol* 2015;111:848-854.
23. Sasako M, Sakuramoto S, Katai H, Kinoshita T, Furukawa H, Yamaguchi T, et al. Five-year outcomes of a randomized phase III trial comparing adjuvant chemotherapy with S-1 versus surgery alone in stage II or III gastric cancer. *J Clin Oncol* 2011;29:4387-4393.
24. Shen L, Shan YS, Hu HM, Price TJ, Sirohi B, Yeh KH, et al. Management of gastric cancer in Asia: resource-stratified guidelines. *Lancet Oncol* 2013;14:e535-547.
25. Shi RL, Chen Q, Yang Z, Pan G, Zhang Z, Wang W, et al. Marital status independently predicts gastric cancer survival after surgical resection—an analysis of the SEER database. *Oncotarget* 2016;7:13228-13235.
26. Shi T, Song X, Liu Q, Yang Y, Yu L, Liu B, et al. Survival benefit of palliative gastrectomy followed by chemotherapy in stage IV gastric signet ring cell carcinoma patients: A large population-based study. *Cancer Med* 2019;8:6010-6020.
27. Shin HB, Lee SH, Son YG, Ryu SW, Sohn SS. Chemoresponse after non-curative gastrectomy for M1 gastric cancer. *World J Surg Oncol* 2015;13:13.
28. Solaini L, Ministrini S, Coniglio A, Cavallari S, Molteni B, Baiocchi GL, et al. How could we identify the 'old' patient in gastric cancer surgery? A single centre cohort study. *Int J Surg* 2016;34:174-179.
29. Song M, Kang D, Yang JJ, Choi JY, Sung H, Lee Y, et al. Age and sex interactions in gastric cancer incidence and mortality trends in Korea. *Gastric Cancer* 2015;18:580-589.

30. Song P, Wu L, Jiang B, Liu Z, Cao K, Guan W. Age-specific effects on the prognosis after surgery for gastric cancer: A SEER population-based analysis. *Oncotarget* 2016;7:48614-48624.
31. Van Cutsem E, Moiseyenko VM, Tjulandin S, Majlis A, Constenla M, Boni C, et al. Phase III study of docetaxel and cisplatin plus fluorouracil compared with cisplatin and fluorouracil as first-line therapy for advanced gastric cancer: a report of the V325 Study Group. *J Clin Oncol* 2006;24:4991-4997.
32. Wu P, Wang P, Ma B, Yin S, Tan Y, Hou W, et al. Palliative gastrectomy plus chemotherapy versus chemotherapy alone for incurable advanced gastric cancer: a meta-analysis. *Cancer Manag Res* 2018;10:4759-4771.
33. Yeh JM, Tramontano AC, Hur C, Schrag D. Comparative effectiveness of adjuvant chemoradiotherapy after gastrectomy among older patients with gastric adenocarcinoma: a SEER-Medicare study. *Gastric Cancer* 2017;20:811-824.

Additional Files

Additional files 1- Stratified analysis of age concerning effects of therapeutic method on OS.

This table provides the detailed data of hazard ratios of OS by four intervention methods based on age stratification.

Additional files 2- Stratified analysis of grade concerning effects of therapeutic method on OS.

This table provides the detailed data of hazard ratios of OS by four intervention methods based on grade stratification.

Additional files 3- Stratified analysis of age concerning effects of therapeutic method on CSS.

This table provides the detailed data of hazard ratios of CSS by four intervention methods based on age stratification.

Additional files 4- Stratified analysis of grade concerning effects of therapeutic method on CSS.

This table provides the detailed data of hazard ratios of CSS by four intervention methods based on grade stratification.

Additional files 5- PRISMA checklist

The PRISMA checklist can help authors check the content integrity and be useful for critical appraisal of this manuscript.

Figures

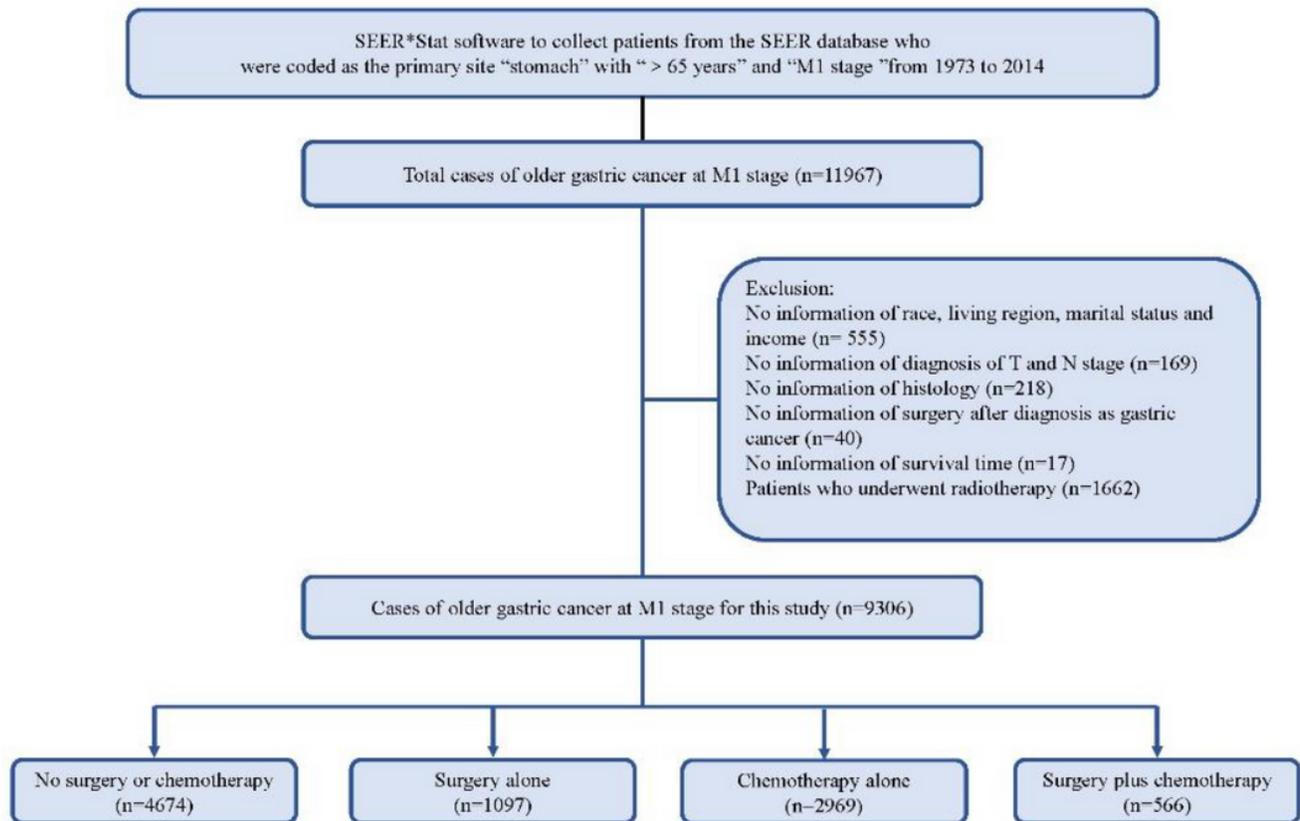


Figure 1

Flow chart of study enrollment and exclusions.

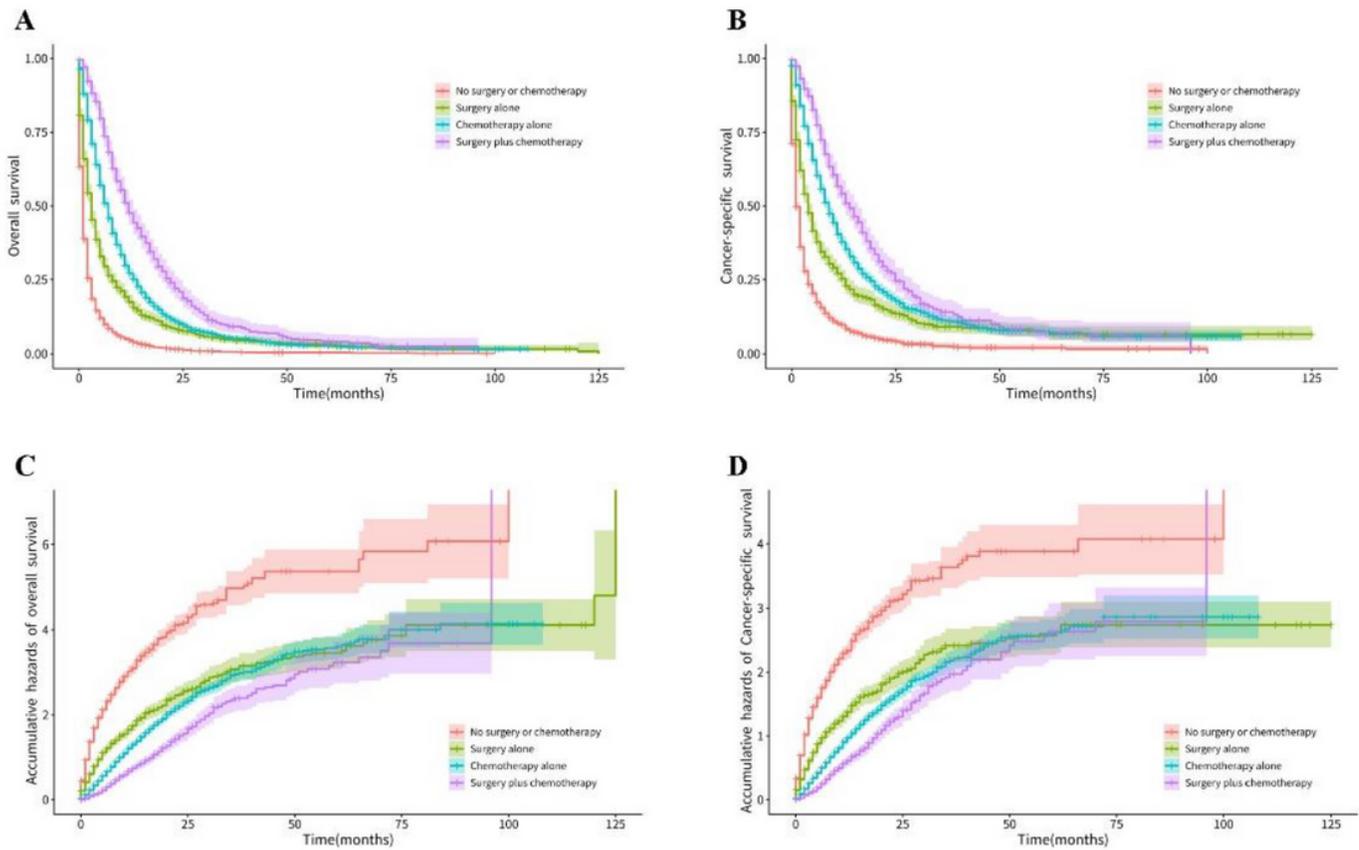


Figure 2

Kaplan-Meier survival analysis of four intervention methods. Overall survival and cancer-specific survival between elderly patients of gastric cancer at \geq stage who received four different intervention methods, $P < 0.001$ (A, B); Accumulative hazards of overall survival and cancer-specific survival between elderly patients of gastric cancer at \geq stage who received four different intervention methods, $P < 0.001$ (C, D).

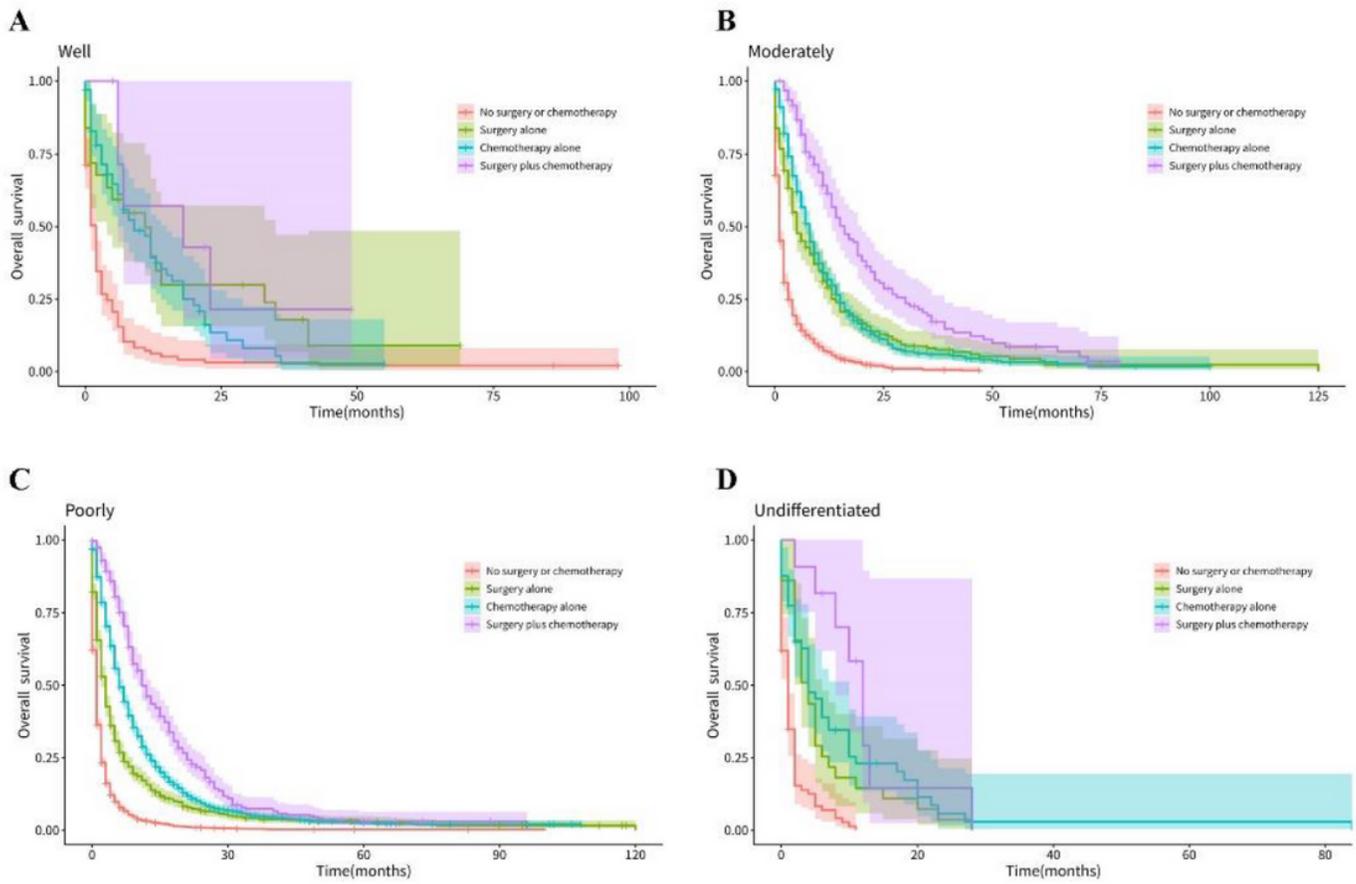


Figure 3

Grade stratification of overall survival. Overall survival between elderly patients of gastric cancer at \square stage who received four different intervention methods were stratified by four grades, well (A), moderately (B), poorly (C), undifferentiated (D).

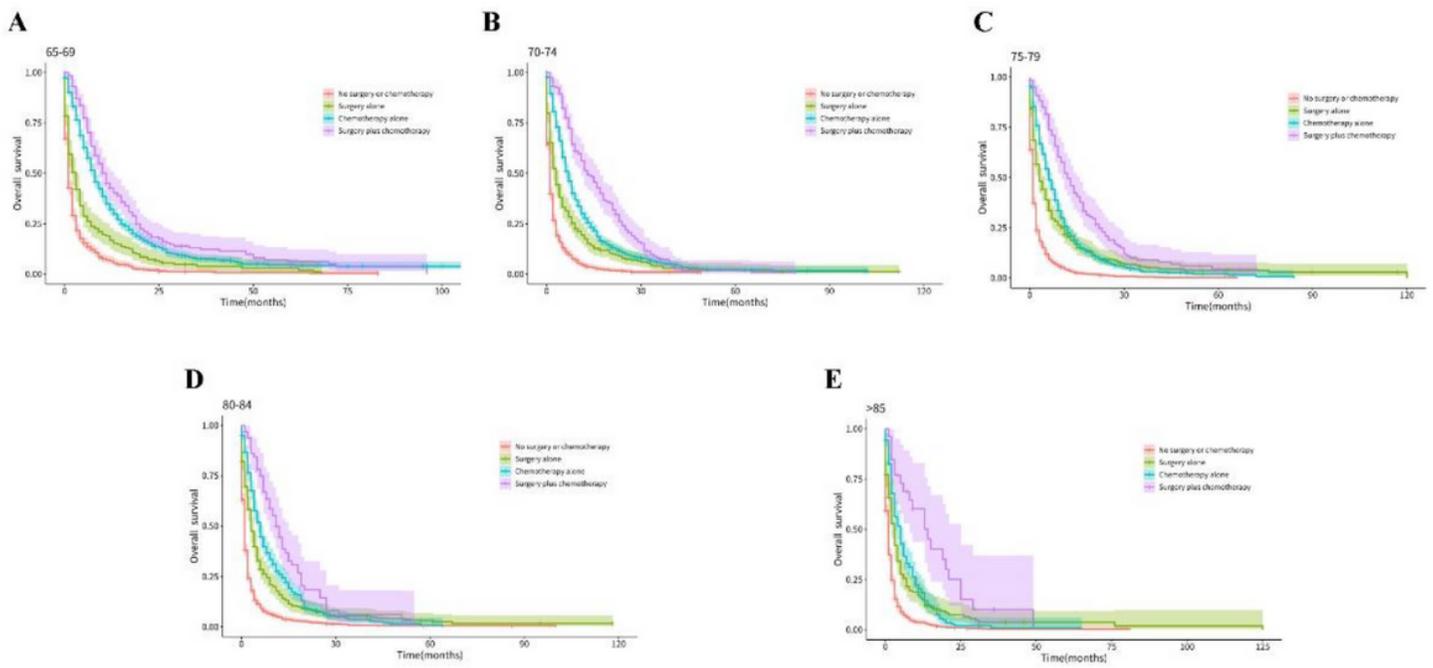


Figure 4

Age stratification of overall survival. Overall survival between elderly patients of gastric cancer at \square stage who received four different intervention methods were stratified by four age, 65-69 (A), 70-74 (B), 75-79 (C), 80-84 (D) and \square 85 (E).

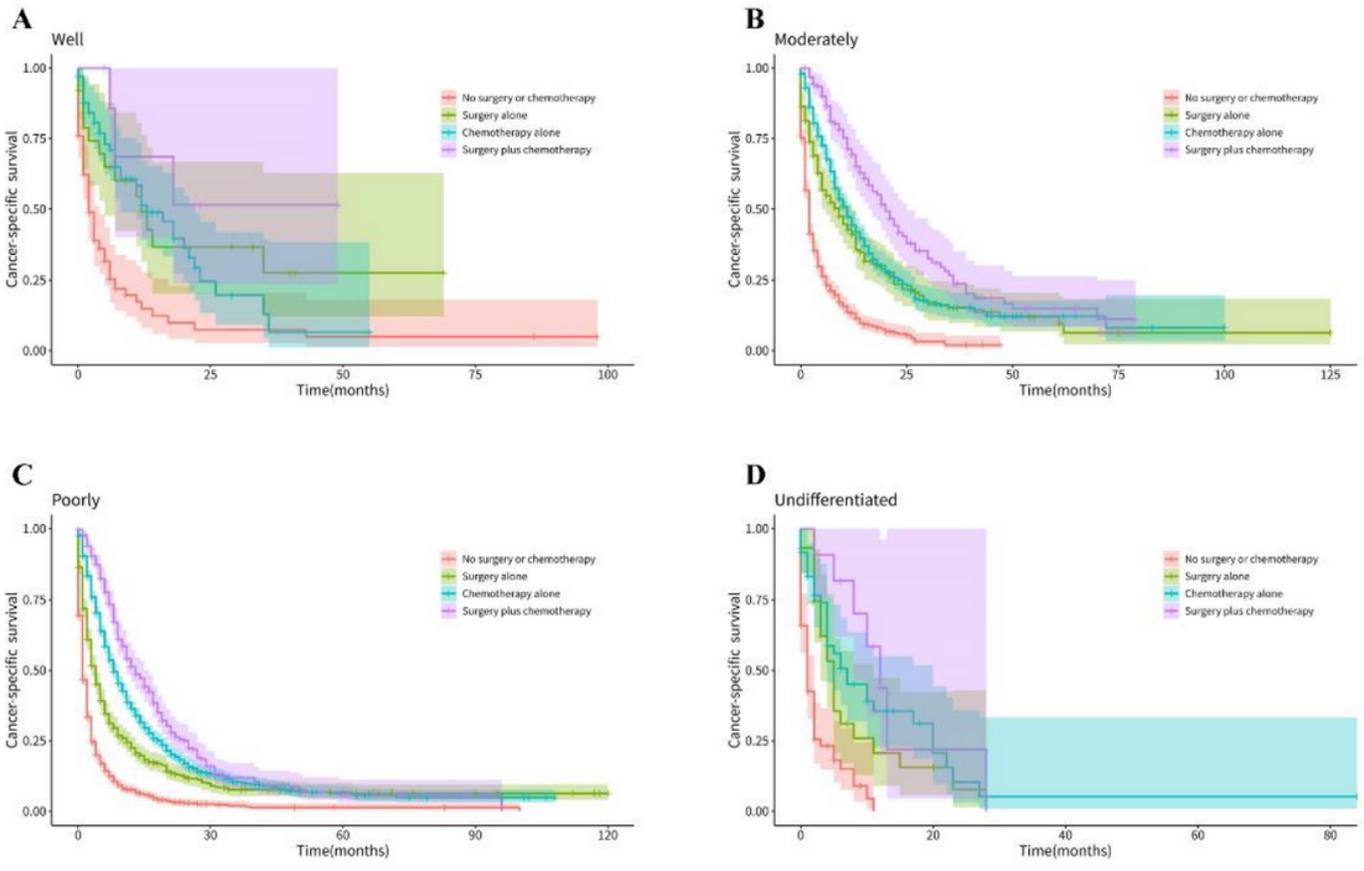


Figure 5

Grade stratification of cancer-specific survival. Cancer-specific survival between elderly patients of gastric cancer at T4 stage who received four different intervention methods were stratified by four grades, well (A), moderately (B), poorly (C), undifferentiated (D).

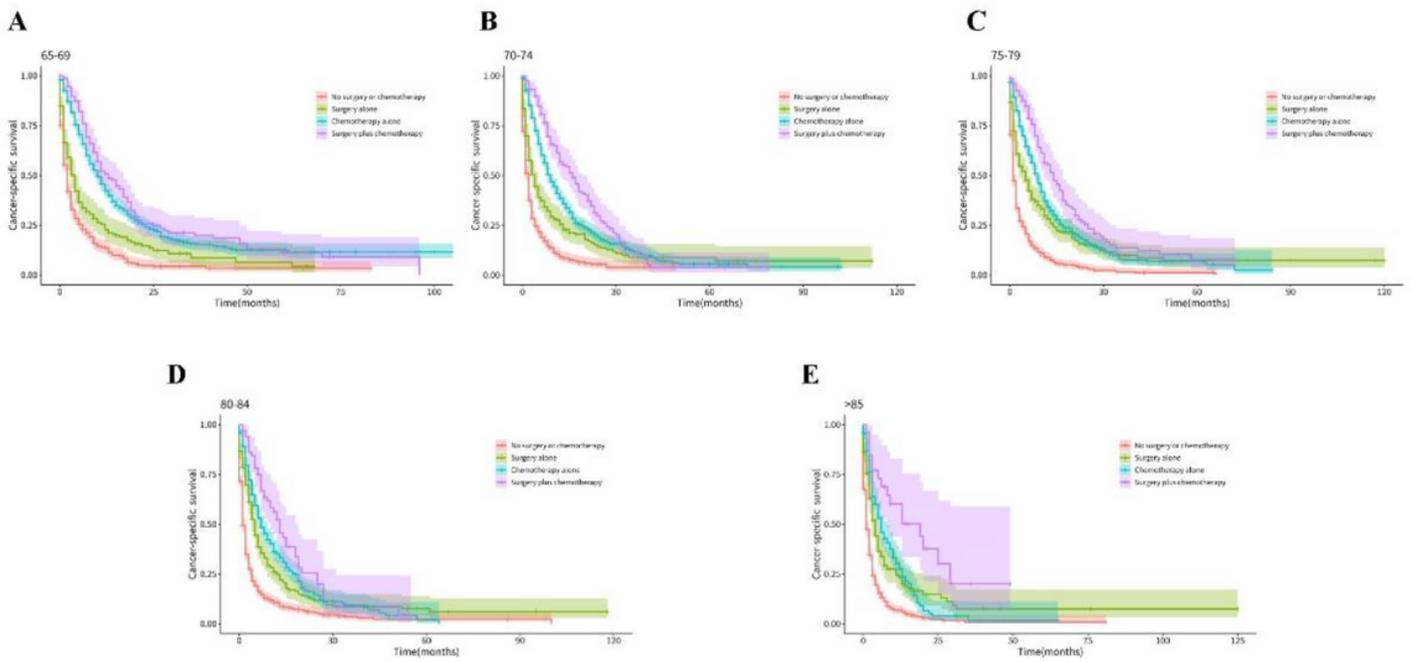


Figure 6

Age stratification of cancer-specific survival. Cancer-specific survival between elderly patients of gastric cancer at \geq stage who received four different intervention methods were stratified by four age, 65-69 (A), 70-74 (B), 75-79 (C), 80-84 (D) and \geq 85 (E).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile3.docx](#)
- [Additionalfile2.docx](#)
- [Additionalfile1.docx](#)
- [Additionalfile5.doc](#)
- [Additionalfile4.docx](#)