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Analysis

Survival benefits of postoperative adjuvant chemotherapy in adults aged ≥ 80 years with locally advanced gastric cancer: insights from a population-based study

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Abstract

Background and aims Postoperative adjuvant chemotherapy in older adults aged ≥ 80 years with locally advanced gastric cancer (LAGC) remains debated owing to concerns over treatment tolerance and limited data. We aimed to assess the effectiveness of postoperative adjuvant chemotherapy in adults aged ≥ 80 years with LAGC using data from the Surveillance, Epidemiology, and End Results database.

Methods and results A total of 2395 patients with LAGC aged ≥ 80 years who underwent radical surgery between 2004 and 2015 were identified. Propensity score matching (1:1) was applied to pair 422 patients receiving adjuvant chemotherapy with 1973 patients who underwent surgery alone. Multivariate logistic regression identified independent predictors of adjuvant chemotherapy, including the period from 2012–2015, pN1–2 and pN3 stages, and radiation therapy. Conversely, age ≥ 85 years predicted decreased chemotherapy use. Cancer-specific survival (CSS) and overall survival (OS) were compared using multivariate Cox analysis, showing significantly longer OS and CSS in the adjuvant chemotherapy group, before and after matching. Subgroup analysis revealed that patients aged 80–84 years and those with N + stages benefited most from adjuvant chemotherapy, whereas patients aged ≥ 90 years did not show significant benefit.

Conclusion Postoperative adjuvant chemotherapy should be considered for patients aged ≥ 80 years with LAGC, especially those with lymph node involvement, as it offers significant survival benefits. However, as age approaches 90 years, the benefits of adjuvant chemotherapy may diminish, warranting more cautious application.

Keywords Adjuvant chemotherapy · Locally advanced gastric cancer · Older adults · SEER database

1 Introduction

Despite a decline in overall incidence in recent decades, gastric cancer (GC) remains the fifth most common cancer and the third leading cause of cancer-related death globally [1]. GC prevalence increases markedly with age, with a median diagnosis age of around 70 years [2]. Over the past several decades, the global population has rapidly aged, and consequently, the burden of GC in older adults has continued to grow [3].

Radical gastrectomy remains the primary therapeutic approach for locally advanced gastric cancer (LAGC) [4]. To improve long-term outcomes, postoperative adjuvant chemotherapy is recommended following curative gastrectomy

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[5, 6]. Advances in anesthesia, operative techniques, and perioperative management have caused a rise in the number of gastrectomies performed in older individuals [7]; however, because of the presence of organ dysfunction and limited life expectancy in these patients, the adjuvant treatment strategy for older adult patients with LAGC is particularly challenging [8]. Additionally, older adults, particularly those aged ≥ 80 years, are also at increased risk of chemotherapeutic toxicity, making them less likely to tolerate standard regimens [9]. Moreover, the current guidelines for postoperative adjuvant treatment of GC are largely based on clinical trials conducted primarily in younger patients, with limited direct evidence addressing older adults. Although some retrospective studies with small sample sizes have evaluated the prognostic value of postoperative adjuvant chemotherapy in LAGC patients aged ≥ 80 years, the benefit in this age group remains uncertain and controversial.

In this context, our study aimed to assess the effectiveness of postoperative adjuvant chemotherapy in patients aged ≥ 80 years with LAGC following curative gastrectomy. Using data from the Surveillance, Epidemiology, and End Results (SEER) database, we conducted a comprehensive, population-based analysis of clinical outcomes in this understudied age group.

2 Methods

2.1 Data source

This study sought to determine the efficacy of postoperative adjuvant chemotherapy in patients aged ≥ 80 years with LAGC who had undergone curative gastrectomy, using data from the SEER database (Incidence-SEER Research Data, 17 registries, November 2022 Sub [2000–2022], released April 2023). The SEER database is a comprehensive, population-based cancer database covering approximately one-third of the U.S. population. Data for this study were extracted using SEER*Stat Software (version 8.3.9). Patients diagnosed between January 2004 and December 2015 were selected for analysis. As the SEER database does not contain personally identifiable data, ethical approval and informed consent were not needed.

2.2 Patient selection and data collection

The inclusion criteria were age > 80 years; histology/behavior codes 8140/3–8147/3, 8210/3–8211/3, 8221/3, 8255/3, 8260/3–8263/3, 8480/3–8481/3, and 8490/3; site codes C16.0–C16.9; patients who underwent radical gastrectomy with a clear surgical approach (Surgery Codes for Stomach codes 30–33, 40–42, 51–52, and 61–62); and a locally advanced stage (T1–2 N+ or T3–4 N0/+, M0). Patients were excluded if they were treated with either preoperative or intraoperative systemic therapy. Other exclusion criteria were patients without a detailed description of the surgery, those who did not undergo radical gastrectomy, and patients with missing baseline or clinicopathological data (e.g., race, site, T stage, N stage, or tumor grade).

The retrieved baseline and clinicopathological information included age at diagnosis, sex, ethnicity, tumor location, histological classification, differentiation grade, TNM stage, type of gastrectomy, chemotherapy, radiotherapy, and follow-up information. The pathological TNM status of patients from 2004 to 2015 was determined using the 6 th or 7 th edition of the American Joint Committee on Cancer (AJCC) Staging Manual. We reevaluated the tumor stage for all patients according to the 7 th edition of the AJCC guidelines. We classified 30–33, 51, and 61 as partial gastrectomies and 40–42, 52, and 62 as total gastrectomies according to the Surgery Codes for Stomach. Codes 61 and 62 were considered combined resections; the others were not. Overall survival (OS) was determined as the period from the original GC diagnosis to the last follow-up or death from any cause. Cancer-specific survival (CSS) spanned from the GC diagnosis to death owing to GC.

2.3 Statistical analysis

Eligible patients with LAGC were divided into two groups: adjuvant chemotherapy and surgery-alone. To minimize confounding variables, propensity score matching (PSM) was employed, balancing factors including age, sex, histological classification, tumor grade, N stage, type of gastrectomy, and radiotherapy. PSM was conducted at a 1:1 matching

ratio using a caliper of 0.01, where the caliper refers to the maximum allowed difference in propensity scores between matched pairs, based on the logit of the propensity score, without replacement.

Before PSM, a multivariate logistic regression analysis was conducted to identify independent risk factors for administering adjuvant chemotherapy in older adult patients with LAGC. OS and CSS were estimated by using the Kaplan–Meier method, with comparisons made via the log-rank test. Independent prognostic factors were determined using the Cox proportional hazards regression model. Data analyses were performed using SPSS (version 26.0) or R software, with statistical significance set at $p < 0.05$.

3 Results

3.1 Patient demographics and characteristics

The study included 2395 patients aged ≥ 80 years with LAGC selected between 2004 and 2015. Among these, 422 patients received adjuvant chemotherapy, while 1973 patients underwent surgery alone. Table 1 shows the demographics and pathological features of the patients. Compared to the surgery-alone group, patients in the adjuvant chemotherapy group were more frequently treated in the 2012–2015 period (29.1% vs. 23.5%), had a higher proportion of males (60.7% vs. 52.2%), exhibited Signet Ring Cell Carcinoma (SRCC) pathology (16.6% vs. 11.0%), underwent total gastrectomy (21.8% vs. 16.9%), presented with N1–2/N3 stage disease (85.6% vs. 71%), and were more likely to receive radiotherapy. Additionally, the number of patients receiving postoperative adjuvant chemotherapy decreased with increasing age. As reported in Table 1, the differences in demographics and pathological features between the matched 212 pairs decreased significantly, resulting in a good balance.

3.2 Factors associated with administering adjuvant chemotherapy in older adults with LAGC

Multivariate logistic regression analyses identified several independent predictors for receiving adjuvant chemotherapy. These included being diagnosed in 2012–2015 (odds ratio [OR]: 1.702; 95% confidence interval [CI]: 1.201–2.411; $p = 0.003$), having pN1–2 (OR: 1.502; 95% CI 1.028–2.194; $p = 0.035$) or pN3 (OR: 2.03; 95% CI 1.335–3.089; $p = 0.001$) stage, and receiving radiation therapy (OR: 55.185, 95% CI 38.593–78.909; $p < 0.001$) were independent predictors of adjuvant chemotherapy administration. Conversely, age 85–89 years (OR: 0.492, 95% CI 0.35–0.691; $p < 0.001$) and ≥ 90 years (OR: 0.307, 95% CI 0.154–0.6095; $p = 0.001$) independently predicted decreased administration of adjuvant chemotherapy (Table 2).

3.3 Effect of adjuvant chemotherapy on survival outcomes in older adult patients with LAGC

Before PSM, Kaplan–Meier curves showed that patients receiving adjuvant chemotherapy had superior OS and CSS compared to those undergoing surgery alone. Specifically, in the adjuvant chemotherapy group, the 1-, 3-, and 5-year OS rates were 73.8%, 48.5%, and 25.2%, respectively, versus 54.1%, 37.5%, and 18.6% in the surgery-alone group ($p < 0.001$) (Fig. 1a). The 1-, 3-, and 5-year CSS rates in the adjuvant chemotherapy group were 77.3%, 52.3%, and 34.4%, respectively, versus 60.9%, 45.9%, and 30.3% for those who had surgery alone ($p < 0.001$) (Fig. 1b).

After PSM, similar outcomes were found among matched patients. The OS rates at 1, 3, and 5 years were 74.0%, 49.0%, and 25.9% in the adjuvant chemotherapy group, compared to 53.0%, 34.5%, and 17.2% in the surgery-alone group (Fig. 1c). Likewise, the CSS rates at 1, 3, and 5 years were 76.8%, 52.8%, and 31.3%, respectively, in the adjuvant chemotherapy group, compared to 58.1%, 40.9%, and 27.9%, respectively, in the surgery-alone group (Fig. 1d).

Multivariate Cox regression analysis was conducted before and after PSM to adjust for potential confounding factors. Before PSM, independent prognostic factors for the OS and CSS included age, sex, race, tumor grade, tumor location, type of gastrectomy, N stage, T stage, radiation use, and adjuvant chemotherapy (Fig. 2a and b). Notably, adjuvant chemotherapy was a significant protective factor for OS (hazard ratio [HR]: 0.68; 95% CI 0.58–0.77; $p < 0.001$) and CSS (HR: 0.71; 95% CI 0.60–0.85; $p < 0.001$) before PSM.

After PSM, the independent factors affecting OS in the matched pairs were age, sex, race, T stage, N stage, radiation use, and adjuvant chemotherapy (HR: 0.63; 95% CI 0.51–0.77; $p < 0.001$) (Fig. 3a). For CSS, the independent factors included age, T stage, N stage, radiation use, and adjuvant chemotherapy (HR: 0.70; 95% CI 0.55–0.89; $p = 0.003$) (Fig. 3b).

Table 1 Demographic and clinicopathological characteristics of older patients with locally advanced gastric cancer

Characteristics	Before PSM		P-value	After PSM		P-value
	Adjuvant chemotherapy group (n = 422) (%)	Surgery-alone group (n = 1973) (%)		Adjuvant chemotherapy group (n = 212) (%)	Surgery-alone group (n = 212) (%)	
Age, years			< 0.001			0.646
80–84	331 (78.4)	1092 (55.3)		159 (75.0)	151 (71.2)	
85–89	80 (19.0)	650 (32.9)		44 (20.8)	52 (24.5)	
90+	11 (2.6)	231 (11.7)		9 (4.2)	9 (4.2)	
Sex			0.002			0.766
Male	256 (60.7)	1030 (52.2)		125 (59.0)	129 (60.8)	
Female	166 (39.3)	943 (47.8)		87 (41.0)	83 (39.2)	
Year at diagnosis			0.048			0.972
2004–2007	164 (38.9)	811 (41.1)		74 (34.9)	72 (34.0)	
2008–2011	135 (32.0)	698 (35.4)		73 (34.4)	73 (34.4)	
2012–2015	123 (29.1)	464 (23.5)		67 (31.6)	65 (30.7)	
Race			0.137			0.595
White	274 (64.9)	1363 (69.1)		141 (66.5)	148 (69.8)	
Black	51 (12.1)	183 (9.3)		24 (11.3)	18 (8.5)	
Other	97 (23.0)	427 (21.6)		47 (22.2)	46 (21.7)	
Location			0.878			0.135
Cardia	44 (10.4)	198 (10.0)		20 (9.4)	31 (14.6)	
Noncardia	378 (89.6)	1775 (90.0)		192 (90.6)	181 (85.4)	
SRCC			0.002			0.611
Yes	352 (83.4)	1755 (89.0)		172 (81.1)	177 (83.5)	
No	70 (16.6)	218 (11.0)		40 (18.9)	35 (16.5)	
Grade			0.136			0.746
Poorly/undifferentiated	301 (71.3)	1331 (67.5)		150 (70.8)	154 (72.6)	
Well/moderately	121 (28.7)	642 (32.5)		62 (29.2)	58 (27.4)	
T stage			0.934			0.855
T1–2	60 (14.2)	279 (14.1)		26 (12.3)	31 (14.6)	
T3	203 (48.1)	964 (48.9)		105 (49.5)	98 (46.2)	
T4a	121 (28.7)	571 (28.9)		61 (28.8)	64 (30.2)	
T4b	38 (9.0)	159 (8.1)		20 (9.4)	19 (9.0)	
N stage			< 0.001			0.583
N0	69 (16.4)	573 (29.0)		45 (21.2)	38 (17.9)	
N1–2	227 (53.8)	960 (48.7)		105 (49.5)	104 (49.1)	
N3a–3b	126 (29.9)	440 (22.3)		62 (29.2)	70 (33.0)	
Type of gastrectomy			0.020			1.000
Partial	330 (78.2)	1640 (83.1)		164 (77.4)	163 (76.9)	
Total	92 (21.8)	333 (16.9)		48 (22.6)	49 (23.1)	
Combined resection			0.715			1.000
No	386 (91.5)	1818 (92.1)		198 (93.4)	198 (93.4)	
Yes	36 (8.5)	155 (7.9)		14 (6.6)	14 (6.6)	
Radiation therapy			< 0.001			1.000
No/unknown	170 (40.3)	1924 (97.5)		168 (79.2)	168 (79.2)	
Yes	252 (59.7)	49 (2.5)		44 (20.8)	44 (20.8)	

PSM: propensity score matching; SRCC: Signet Ring Cell Carcinoma

Table 2 Multivariate logistic analyses of predictive factors for adjuvant chemotherapy administration in older patients with LAGC

	OR	95% CI	P-value
Age, years			
80–84	Reference		
85–89	0.492	0.35–0.691	< 0.001
90+	0.307	0.154–0.609	0.001
Sex			
Male	Reference		
Female	0.869	0.652–1.157	0.336
Year at diagnosis			
2004–2007	Reference		
2008–2011	0.899	0.638–1.265	0.541
2012–2015	1.702	1.201–2.411	0.003
N stage			
N0	Reference		
N1–2	1.502	1.028–2.194	0.035
N3a–3b	2.03	1.335–3.089	0.001
Type of gastrectomy			
Partial	Reference		0.063
Total	1.394	0.982–1.979	
Radiation therapy			
No/unknown	Reference		
Yes	55.185	38.593–78.909	< 0.001

OR: odds ratio; CI: confidence interval

3.4 Subgroup analysis of the effect of adjuvant chemotherapy on OS and CSS

The impact of adjuvant chemotherapy on OS and CSS was further explored through subgroup analysis with stratification (Figs. 4 and 5). For different age groups, adjuvant chemotherapy provided benefits to the OS and CSS of patients aged 80–84 years at diagnosis. Among those aged 85–89 years at diagnosis, adjuvant chemotherapy was linked to improved OS, although no significant effect was observed on CSS. In patients aged 90 and above, adjuvant chemotherapy did not improve either OS or CSS. Additionally, subgroup analyses by sex, SRCC, and combined resection indicated significantly higher OS and CSS rates in the adjuvant chemotherapy group compared to the surgery-alone group. However, in the subgroup analysis of race, tumor location, and type of gastrectomy, adjuvant chemotherapy did not improve OS or CSS among groups with fewer cases.

Subgroup analysis of T stage for all patients showed that the OS rate was significantly higher in the adjuvant chemotherapy group compared to the surgery-alone group. The CSS rate of the adjuvant chemotherapy group was notably higher than that of the surgery-alone group in patients with T1–2 and T4 stages and tended to be higher in those with T3 stage. In terms of N stage, OS and CSS rates were significantly greater for patients with the N+ (N1–3) stage in the adjuvant chemotherapy group, whereas no significant differences were found for patients with the N0 stage.

4 Discussion

Our analysis found that adjuvant chemotherapy significantly improved the prognosis of older adult patients with LAGC. Moreover, we found that, within the subpopulations of patients with lymph node involvement (N+ stage), those who received postoperative adjuvant chemotherapy demonstrated greater benefits than those who did not. Therefore, adjuvant chemotherapy is advisable for older adult patients with LAGC who have undergone gastrectomy, particularly for those with lymph node involvement. However, in the subgroup analyses based on age, adjuvant chemotherapy did not significantly improve the OS and CSS of patients aged ≥ 90 years. As age approaches 90 years,

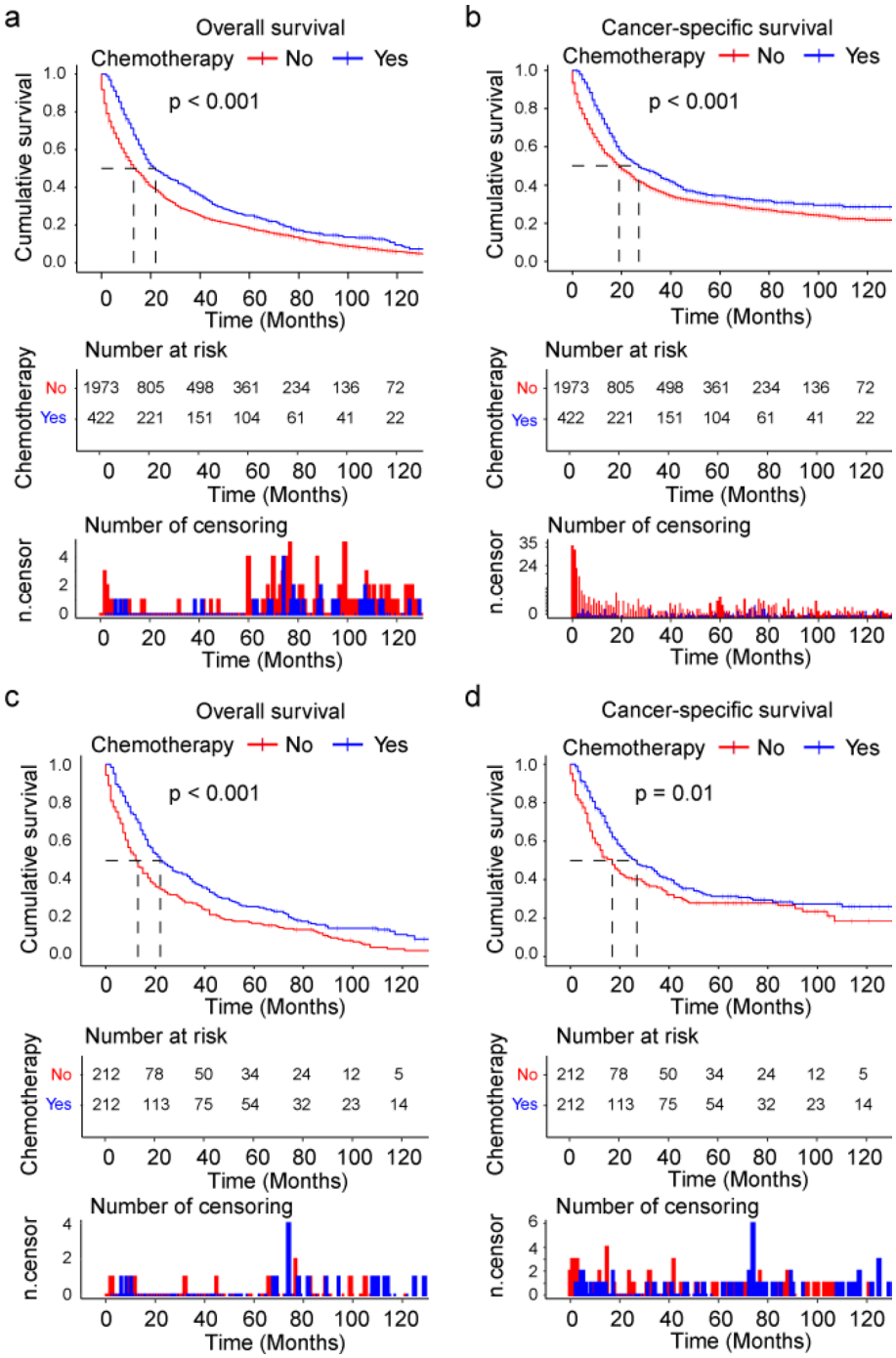


Fig. 1 Comparison of survival curves between the adjuvant chemotherapy and surgery-alone groups: **a** OS before PSM; **b** CSS before PSM; **c** OS after PSM; **d** CSS after PSM. Adjuvant chemotherapy showed significantly superior OS and CSS compared to surgery alone, with $p < 0.001$ for OS (**a**, **c**) and CSS (**b**) before PSM, and $p = 0.01$ for CSS (**d**) after PSM. OS: overall survival; CSS: cancer-specific survival; PSM: propensity score matching

the benefits of adjuvant chemotherapy may gradually decrease, necessitating a more careful consideration of its application. Alternative treatment strategies, such as less aggressive chemotherapy regimens or supportive care, should be considered for this group.

Radical surgery combined with postoperative adjuvant chemotherapy is a key component of the standardized treatment for LAGC based on randomized controlled trials and meta-analyses [5, 6]. In the ACTSGC trial, postoperative adjuvant S-1 treatment after gastrectomy improved relapse-free survival and OS in GC patients [10, 11]. The CLASSIC trial showed increased survival in patients receiving adjuvant therapy with capecitabine plus oxaliplatin compared to those undergoing surgery alone [12, 13]. Furthermore, several meta-analyses showed that postoperative adjuvant chemotherapy is significantly associated with benefits for OS and disease-free survival [14–16]. However, the ACTSGC trial included only patients under 80 years. Although the CLASSIC trial included patients without an upper age limit, the mean age in the

a

Variable	Count	Percent	HR (95%CI)	P value
Age,years				
80–84	1423	59.4	Reference	
85–89	730	30.5	1.24(1.13–1.36)	<0.001
90~	242	10.1	1.50(1.3–1.73)	<0.001
Sex				
Male	1286	53.7	Reference	
Female	1109	46.3	0.84(0.76–0.91)	<0.001
Race				
White	1637	68.4	Reference	
Black	234	9.8	1.01(0.87–1.17)	0.846
Other	524	21.9	0.76(0.69–0.85)	<0.001
Location				
Cardia	242	10.1	Reference	
Noncardia	2153	89.9	0.84(0.73–0.97)	0.019
Type of gastrectomy				
Patital	1970	82.3	Reference	
Total	425	17.7	1.17(1.04–1.31)	0.006
Grade				
Poorly/undifferentiated	1632	68.1	Reference	
Well/Moderately	763	31.9	0.85(0.77–0.93)	<0.001
SRCC				
No	2107	88	Reference	
Yes	288	12	1.09(0.95–1.24)	0.208
T stage				
T1–2	339	14.2	Reference	
T3	1167	48.7	1.35(1.18–1.54)	<0.001
T4a/4b	889	37.1	1.89(1.65–2.17)	<0.001
N stage				
N0	642	26.8	Reference	
N1–2	1187	49.6	1.48(1.33–1.64)	<0.001
N3a–3b	566	23.6	2.24(1.97–2.54)	<0.001
Radiation				
No	2094	87.4	Reference	
Yes	301	12.6	0.9(0.77–1.06)	0.192
Chemotherapy				
No	1973	82.4	Reference	
Yes	422	17.6	0.67(0.58–0.77)	<0.001

b

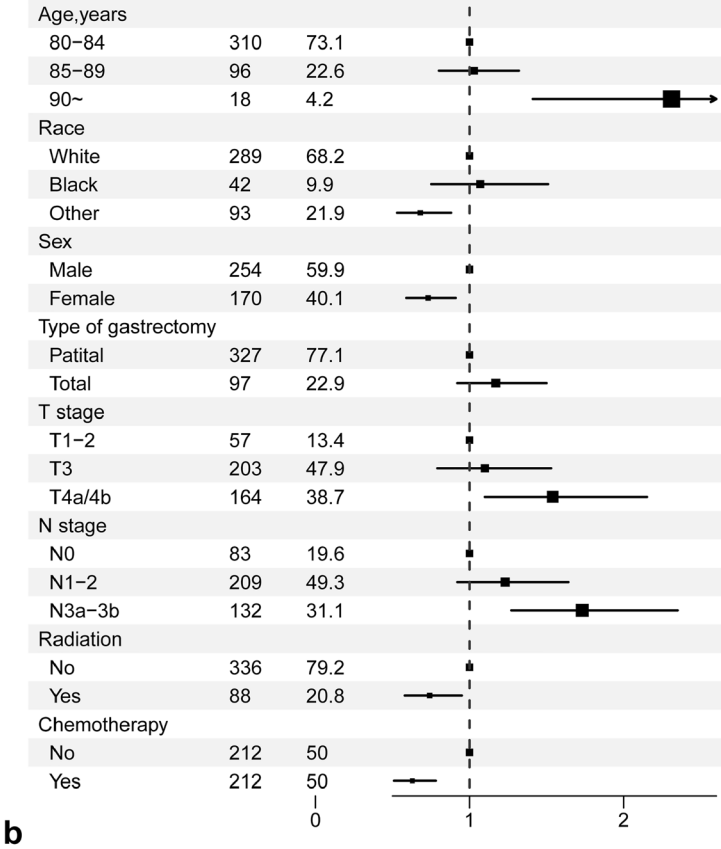
Variable	Count	Percent	HR (95%CI)	P value
Age,years				
80–84	1423	59.4	Reference	
85–89	730	30.5	1.16(1.04–1.30)	0.008
90~	242	10.1	1.35(1.14–1.61)	<0.001
Race				
White	1637	68.4	Reference	
Black	234	9.8	1.04(0.87–1.23)	0.690
Other	524	21.9	0.74(0.65–0.84)	<0.001
Location				
Cardia	242	10.1	Reference	
Noncardia	2153	89.9	0.78(0.66–0.91)	0.002
Type of gastrectomy				
Patital	1970	82.3	Reference	
Total	425	17.7	1.18(1.04–1.34)	0.013
Grade				
Poorly/undifferentiated	1632	68.1	Reference	
Well/Moderately	763	31.9	0.80(0.71–0.90)	<0.001
SRCC				
No	2107	88	Reference	
Yes	288	12	1.08(0.93–1.25)	0.313
T stage				
T1–2	339	14.2	Reference	
T3	1167	48.7	1.58(1.33–1.89)	<0.001
T4a/4b	889	37.1	2.50(2.10–2.96)	<0.001
N stage				
N0	642	26.8	Reference	
N1–2	1187	49.6	1.79(1.57–2.05)	<0.001
N3a–3b	566	23.6	2.74(2.35–3.19)	<0.001
Radiation				
No	2094	87.4	Reference	
Yes	301	12.6	0.78(0.64–0.95)	0.013
Chemotherapy				
No	1973	82.4	Reference	
Yes	422	17.6	0.72(0.61–0.85)	<0.001

Fig. 2 Forest plot of HRs for factors from multivariate Cox proportional hazards analysis of survival before PSM: **a** OS and **b** CSS. Before PSM, adjuvant chemotherapy was a significant protective factor for OS (HR: 0.68; 95% CI 0.58–0.77; $p < 0.001$) and CSS (HR: 0.71; 95% CI 0.60–0.85; $p < 0.001$). OS: overall survival; CSS: cancer-specific survival; PSM: propensity score matching; SRCC: Signet Ring Cell Carcinoma; HR: Hazard ratio; CI: confidence interval

Fig. 3 Forest plot of HRs for factors from multivariate Cox proportional hazards analysis of survival after PSM: **a** OS and **b** CSS. After PSM, adjuvant chemotherapy was a significant protective factor for OS (HR: 0.63; 95% CI 0.51–0.77; $p < 0.001$) and CSS (HR: 0.70; 95% CI 0.55–0.89; $p = 0.003$). OS: overall survival; CSS: cancer-specific survival; PSM: propensity score matching; HR: Hazard ratio; CI: confidence interval

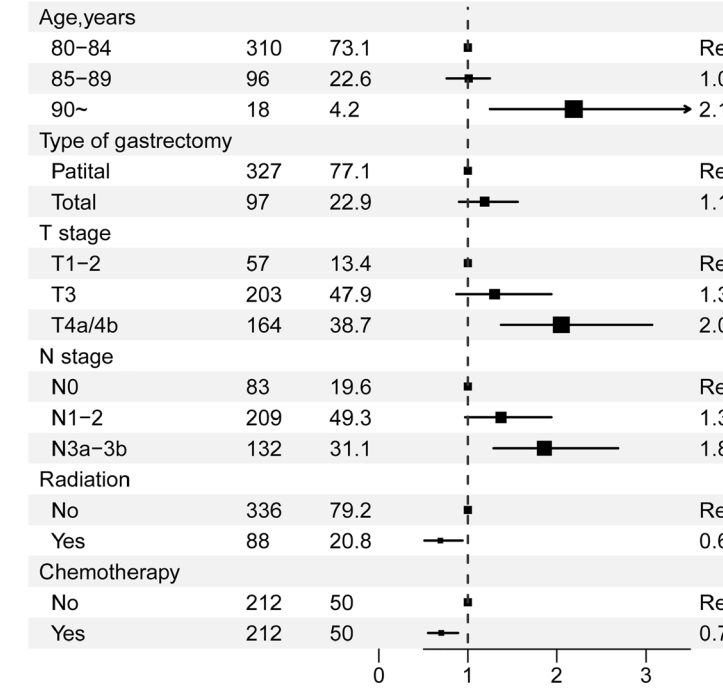
a

Variable	Count	Percent	HR (95%CI)	P value
Age,years				
80–84	310	73.1	Reference	
85–89	96	22.6	1.03(0.80–1.32)	0.820
90~	18	4.2	2.31(1.41–3.80)	0.001
Race				
White	289	68.2	Reference	
Black	42	9.9	1.07(0.75–1.51)	0.721
Other	93	21.9	0.68(0.53–0.88)	0.004
Sex				
Male	254	59.9	Reference	
Female	170	40.1	0.73(0.59–0.91)	0.004
Type of gastrectomy				
Patital	327	77.1	Reference	
Total	97	22.9	1.17(0.92–1.50)	0.208
T stage				
T1–2	57	13.4	Reference	
T3	203	47.9	1.10(0.79–1.53)	0.564
T4a/4b	164	38.7	1.54(1.10–2.15)	0.012
N stage				
N0	83	19.6	Reference	
N1–2	209	49.3	1.23(0.92–1.64)	0.155
N3a–3b	132	31.1	1.73(1.27–2.35)	0.001
Radiation				
No	336	79.2	Reference	
Yes	88	20.8	0.74(0.58–0.95)	0.020
Chemotherapy				
No	212	50	Reference	
Yes	212	50	0.63(0.51–0.78)	<0.001



b

Variable	Count	Percent	HR (95%CI)	P value
Age,years				
80–84	310	73.1	Reference	
85–89	96	22.6	1.01(0.76–1.25)	0.947
90~	18	4.2	2.19(1.25–3.84)	0.006
Type of gastrectomy				
Patital	327	77.1	Reference	
Total	97	22.9	1.19(0.9O–1.56)	0.225
T stage				
T1–2	57	13.4	Reference	
T3	203	47.9	1.30(0.87–1.94)	0.204
T4a/4b	164	38.7	2.05(1.37–3.07)	<0.001
N stage				
N0	83	19.6	Reference	
N1–2	209	49.3	1.37(0.97–1.94)	0.072
N3a–3b	132	31.1	1.86(1.29–2.69)	0.001
Radiation				
No	336	79.2	Reference	
Yes	88	20.8	0.69(0.51–0.94)	0.019
Chemotherapy				
No	212	50	Reference	
Yes	212	50	0.70(0.55–0.89)	0.003



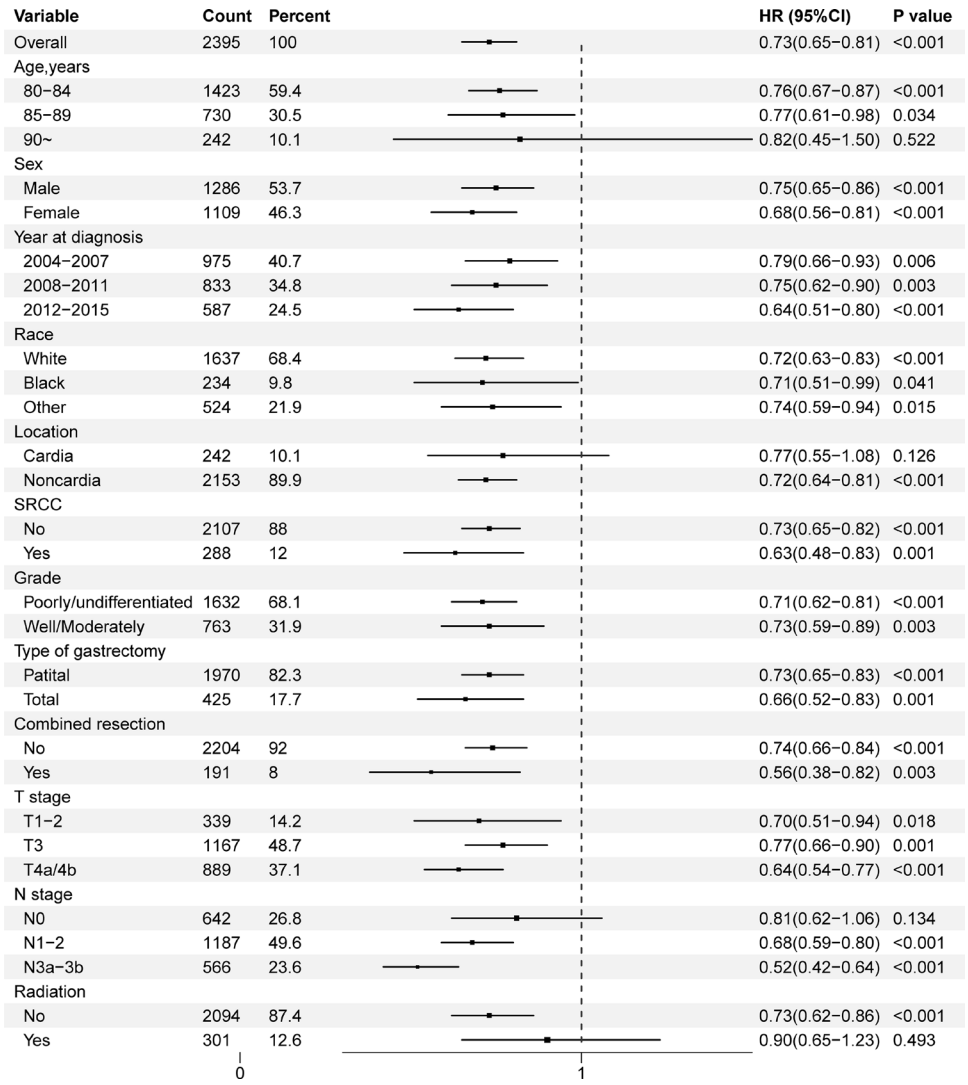


Fig. 4 Subgroup analysis of the effects of adjuvant chemotherapy on overall survival. HR: hazard ratio; CI: confidence interval

adjuvant chemotherapy group was 56.1 years. As a result, although these randomized controlled trials revealed survival benefits of adjuvant chemotherapy, they did not provide solid evidence for adjuvant chemotherapy in older adult patients with GC, especially those aged ≥ 80 years.

Many studies have highlighted age-dependent biological differences in GC among older adults. Although different results have been reported, GC-related survival is significantly lower in older patients than in younger ones [17, 18]. Older patients with GC are predominantly male, show a higher prevalence of tumors in the distal third of the stomach, and more frequently present with well- or moderately-differentiated tumors compared to younger patients [19]. Histologically, older adults with GC have mainly intestinal-type tumors, particularly papillary adenocarcinomas. Additionally, the Cancer Genome Atlas network's molecular profiling found that older patients with GC have a more frequent subtype of microsatellite instability [16, 20]. Transcriptomic analyses indicated that the processes related to resistance to chemotherapy with DNA-damaging drugs, including those involved in DNA repair and the p53 system, were altered in older adults with GC [21]. Physiological changes associated with aging, such as pharmacodynamic variability, reduced organ function, and diminished physical and cognitive capabilities, necessitate individualized treatment approaches [22]. Studies have shown that older patients have a higher incidence of serious postoperative complications [23–26], making them less likely to receive standard treatment for GC compared to younger patients [8, 27, 28]. Our study found that patients with lymph node involvement (N+ stage) and higher T stage were more likely to receive adjuvant therapy, whereas increased age was independently associated with reduced administration of postoperative adjuvant chemotherapy.

In the absence of relevant randomized controlled trials, several retrospective studies have attempted to verify the effectiveness of adjuvant chemotherapy in older patients with LAGC [29]. However, only a few older patients were

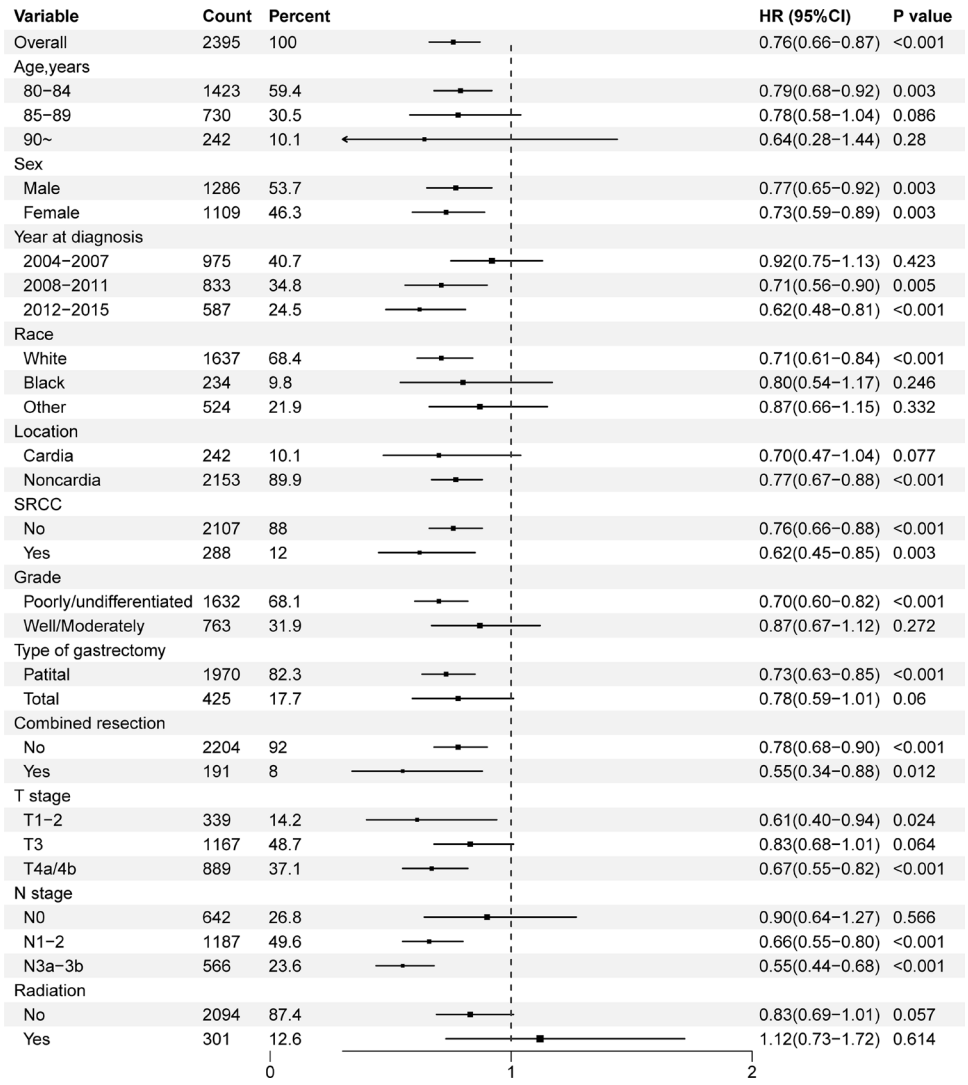


Fig. 5 Subgroup analysis of the effects of adjuvant chemotherapy on cancer-specific survival. HR: hazard ratio; CI: confidence interval

included in most of these studies, with the age group varying among different studies. Some studies set 65 years as the cutoff for older adult patients [30, 31], whereas others chose 70 or 75 years [28, 32–34]. Evidence for patients aged > 80 years is scarce and inconsistent. Jeong et al. found no OS benefit from postoperative adjuvant chemotherapy in patients aged ≥ 75 years with GC [33]. Furthermore, Schendel et al. assessed multimodality therapy and surgery only for patients aged ≥ 75 years with non-metastatic GC who could receive standard-of-care multimodality therapy; they found no survival benefit over surgery alone [28]. Guo et al. defined 75 years as the cutoff age for the definition of older adults and found that adjuvant chemotherapy provided no benefit for patients with stage II GC [35]. On the contrary, Chan et al. found that postoperative adjuvant chemotherapy improved OS and CSS in patients aged ≥ 65 years with LAGC. Further subgroup analysis found similar outcomes in patients aged > 80 years [36]. Moreover, Shih et al. reported that the administration of adjuvant chemotherapy improved OS and disease-free survival in patients ≥ 70 years with LAGC [34]. Similarly, our study showed that adjuvant chemotherapy provided OS and CSS benefits in patients aged ≥ 80 years with LAGC. Although subgroup analyses found no significant benefit of adjuvant chemotherapy for patients aged ≥ 90 years, the findings should be evaluated cautiously because the subgroups had small sample sizes.

While our study found that adjuvant chemotherapy significantly improved the prognosis of older adults aged ≥ 80 years with LAGC, careful patient selection remains essential due to the broad variability in health status within this population. Older patients often present with multiple comorbidities and reduced physiological reserves, which can make it challenging for them to tolerate aggressive treatments. Treatment decisions should take into account factors such as clinicopathological characteristics, pre-treatment medical and nutritional status, quality of life, and long-term outcomes, particularly quality of life [37]. Rather than relying solely on chronological age, a subjective assessment of biological age

is essential to evaluate a patient's ability to tolerate chemotherapy [38]. A comprehensive geriatric assessment (CGA), which focuses on functional age, is crucial for predicting chemotherapy tolerance and guiding treatment decisions [39]. However, a key limitation of our study is the lack of detailed geriatric data in the SEER database, including comorbidities, nutritional status, and physical function. This absence of data meant that patient selection in our analysis was based primarily on age, limiting the ability to conduct more refined, individualized treatment planning.

CGA is particularly important for identifying frailty in elderly cancer patients, which is associated with a higher risk of complications, chemotherapy intolerance, and mortality. Incorporating CGA into clinical practice could improve treatment decisions by emphasizing functional age rather than chronological age, enabling more tailored treatment strategies that better meet the needs of individual patients [40]. Studies suggest that elderly patients can benefit from both radical and palliative treatments when therapies are adjusted to their functional status, similar to younger patients [19]. Therefore, it is vital to integrate geriatric assessments into clinical practice, and future research focusing on elderly patients with appropriate geriatric evaluations is needed to establish clearer, more personalized treatment guidelines for this often-overlooked population.

To our knowledge, this is the first study to evaluate the influence of postoperative adjuvant chemotherapy on the OS and CSS of patients aged ≥ 80 years after gastrectomy. However, this study has several limitations. First, detailed information on treatment is not available in the SEER database, including chemotherapy regimens (drugs and doses), courses, and toxicities, which are important for evaluating the benefits and risks of chemotherapy. Second, geriatric assessments that may affect the use of aggressive treatment were not included in the SEER database, including comorbidities, nutritional status, and physical functional status. Third, although PSM was applied to reduce bias, the lack of randomization could have led to significant differences in the distribution of prognostic factors between treatment groups. These common drawbacks of retrospective or surveillance studies may reduce the reliability of this study's outcomes.

Our study showed that adjuvant chemotherapy significantly improved the prognosis of older adults aged ≥ 80 years with LAGC, especially for those with lymph node involvement, compared to surgery alone. However, as age approaches 90 years, the benefits of adjuvant chemotherapy may diminish, necessitating a more careful consideration of its application. Physicians should balance adjuvant chemotherapy's potential benefits and risks in older adult patients with LAGC. In the future, prospective studies focusing on patients aged ≥ 80 years with LAGC, combined with appropriate geriatric evaluations, should be advocated to better tailor treatment strategies for this population.

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Data availability Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate The SEER database is publicly accessible and provides patient data without specific identification, so ethics approval and informed consent were not required.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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