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RESEARCH

Adjuvant chemotherapy may have no significant survival benefit in older patients with stage II/III gastric cancer: a multicenter retrospective study

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Abstract

Aim Postoperative adjuvant chemotherapy is known to enhance cure rates and is thus recommended for stages pII to pIII. However, specific guidelines for such treatment in elderly gastric cancer (GC) patients are currently lacking. This study examines the impact of adjuvant chemotherapy on the postoperative survival of these patients.

Methods We reviewed a total of 7749 patients with GC who underwent radical gastrectomy at Zhejiang Cancer Hospital and Fujian Cancer Hospital from January 2007 to December 2019. We conducted univariate and multivariate Cox regression analyses to investigate the impact of clinicopathological factors on overall survival (OS) and cancer-specific survival (CSS) in these patients. Additionally, we created a meta-analysis forest plot and employed propensity score matching (PSM) to mitigate confounding bias.

Results Age and adjuvant chemotherapy were independent risk factors for OS and CSS. Stratified analysis based on chemotherapy use revealed a statistically significant difference in OS and CSS between younger patients who did and did not receive adjuvant chemotherapy. In contrast, no significant differences in OS and CSS were observed between older patients with or without adjuvant chemotherapy. These findings remained consistent after propensity score matching (PSM).

Conclusions Age and adjuvant chemotherapy are independent risk factors for OS and CSS in patients with stage II/III GC; for patients with stage II/III gastric cancer aged ≥ 75 years, shared decision-making should be made taking into account functional status and comorbidities, rather than conventional adjuvant chemotherapy.

Keywords Gastric cancer · Adjuvant chemotherapy · Elderly patients

Introduction

Globally, gastric cancer (GC) ranks as the fifth most prevalent malignancy and the fourth leading cause of cancer mortality according to 2022 National Cancer Statistics(Chen et al. 2016; Sung et al. 2020). In China, GC represents the second leading cause of cancer-related mortality in the elderly population. This demographic shift, driven by accelerated aging and extended longevity, has resulted in a growing cohort of geriatric cancer patients, imposing substantial burden on healthcare infrastructure (Ju et al. 2023). China's rapidly aging population has established geriatric cohorts as the primary contributors to the national cancer burden, a trend projected to intensify with ongoing demographic transitions (Ju et al. 2023; Vollset et al. 2020).

In East Asia, radical gastrectomy with D2 lymphadenectomy has become the standard procedure for gastric cancer.

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Postoperative adjuvant chemotherapy can improve the postoperative cure rate, so it is recommended for the pII to pIII stage (Takayama and Tsuji 2023). Postoperative adjuvant chemotherapy is a recommended treatment based on prospective clinical studies, such as the S-1 Gastric Cancer Adjuvant Chemotherapy Trial (ACTS-GC) (Sakuramoto et al. 2007; Sasako et al. 2011), Capecitabine and Oxaliplatin Adjuvant Study in Gastric Cancer (CLASSIC) (Bang et al. 2012; Noh et al. 2014), S-1 Docetaxel versus S-1 Alone Adjuvant Chemotherapy Trial (JACCRO GC-07) (Yoshida et al. 2019) and SOX Adjuvant Chemotherapy for Gastric Cancer studies (ARTIST 2), which demonstrated that adjuvant chemotherapy improved disease-free survival (DFS) and overall survival (OS) in stage II/III gastric cancer patients undergoing D2 gastrectomy (Park et al. 2021). However, the existing standard chemotherapy regimens are primarily developed in non-frail, non-comorbid patients with a median age of less than 65 years, and despite the participation of selected older adults, they cannot be considered fully representative of the older population, and older patients are underrepresented in clinical studies (Pitkala and Strandberg 2022; Thake and Lowry 2017).

To date, there are no specific guidelines for adjuvant chemotherapy in elderly patients with gastric cancer. Older patients have a short life expectancy, many comorbidities, and a high risk of treatment-related complications, and guidelines based on clinical trial results in younger patients are not directly applicable to the treatment of older cancer patients (Aapro et al. 2005). Consequently, the objective of this study is to examine the effects of adjuvant chemotherapy on postoperative survival in elderly patients with gastric cancer, thereby providing guidance to clinicians in selecting appropriate treatment strategies for these patients to optimize their outcomes.

Materials and methods

Selection criteria and patients

We reviewed a total of 7749 gastric cancer patients who underwent radical gastrectomy at Zhejiang Cancer Hospital and Fujian Cancer Hospital from January 2007 to December 2019. All patients underwent radical gastrectomy followed by adjuvant chemotherapy, including monotherapy and combination therapy. Histopathological examination was performed according to AJCC Phase 8 system. The inclusion criteria of this study were: (1) Radical gastrectomy for gastric cancer; (2) Patients with primary gastric cancer at stages pII/III; (3) Adjuvant chemotherapy after operation; (4) Complete clinicopathological data and follow-up data (regular outpatient follow-up and telephone follow-up). Exclusion criteria were: (1) No radical operation or palliative operation was performed for gastric cancer; (2) Patients with primary gastric cancer at stages pI/IV; (3) Neoadjuvant therapy; (4) Incomplete clinical and pathological data; (5) Combined with other malignant tumors; (6) Gastric stump cancer, recurrent cancer and special types of gastric tumors. The design flow chart is shown in Fig. 1, and a total of 5243 patients were eventually included in this study. This study was designed as a multicenter, retrospective study approved by the Medical Ethics Committee of Zhejiang Cancer Hospital (IRB-2022-371).

Clinicopathological characteristics

According to the pathological classification from the 8th edition of the International Union for Cancer Control (UICC) guidelines, a range of clinicopathological data was gathered, including patient age, sex, body mass index (BMI), tumor location, degree of differentiation, pathological type, pT stage, pN stage, nerve invasion, vascular cancer thrombus, surgical method, tumor marker levels, and the presence or absence of postoperative adjuvant chemotherapy. Overall survival (OS) and cancer-specific survival (CSS) served as the primary outcome measures of this study.

Statistical analysis

Clinical and pathological data were analyzed statistically using SPSS software (Version 25.0, IBM Corp, Armonk, NY, USA) and the *Survival*, *Forestplot* and *MatchIt* packages in R 4.2.3(https://www.r-project.org/). In all tests, $P < 0.05$ was considered statistically significant. Classification data were analyzed using the χ^2 test or Fisher's exact test. Survival rates were assessed using the Log-rank test and Kaplan–Meier method. The *Survival* package was utilized to investigate the influence of clinicopathological factors on OS and CSS in GC patients through univariate and multivariate COX regression analysis, the *Forestplot* package was employed to generate forest plots from multivariate analysis results, and the *MatchIt* package was utilized for propensity score matching (PSM) to mitigate confounding bias.

Follow-up

All patients were reviewed every 3 months in the first 2 years after surgery and every 3 to 6 months in the 2 to 5 years after surgery. Follow-up methods such as outpatient review and telephone calls were adopted in December 2023.

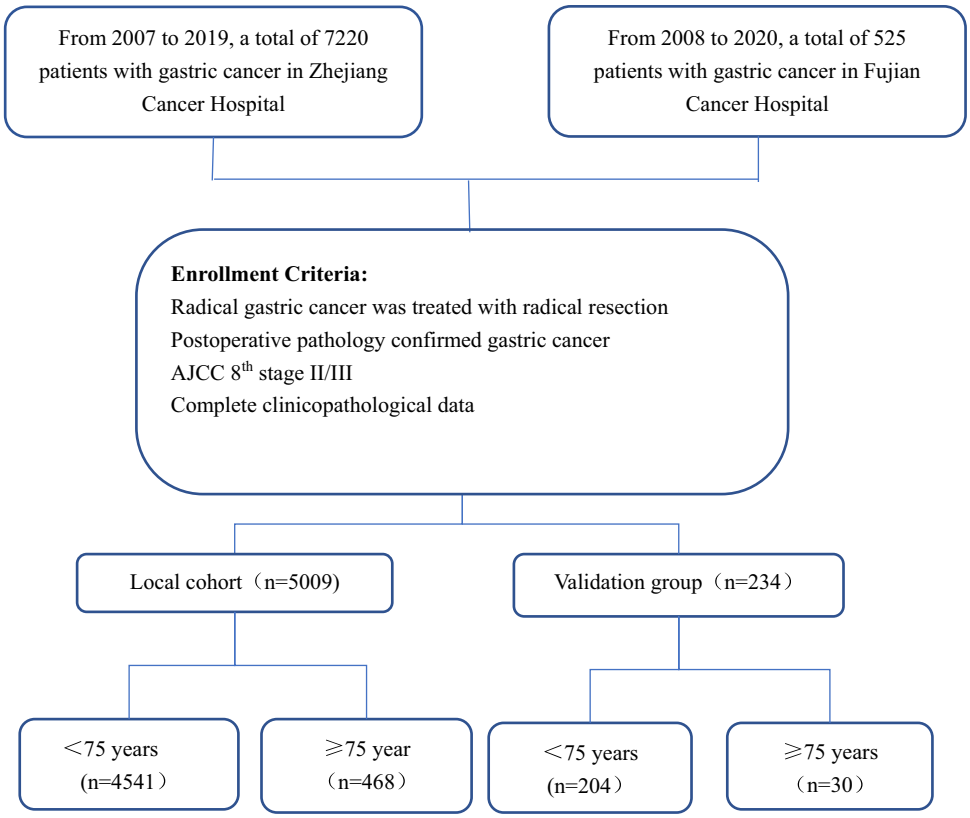

Fig. 1 Flow diagram of this study

Results

Baseline characteristics

This study involved 2 independent cohorts of GC patients, the local cohort (n = 5009) and the Fujian cohort (n = 234). The median age of GC patients meeting the inclusion criteria at diagnosis in the local cohort was 62 years (ranging from 19 to 92 years), while in the Fujian cohort, it was 59 years (ranging from 23 to 83 years). We divided GC patients into two age groups: those aged ≥ 75 years and those aged < 75 years. The clinicopathologic features of the local and Fujian cohorts are detailed in Table S1.

Comparison of clinicopathologic features between young and elderly patient groups

The elderly group showed lower BMI (P < 0.001), with a higher proportion of tumors located in the upper stomach (P < 0.001), the incidence of signet ring cell carcinoma was lower (P = 0.008), and the degree of tumor differentiation was higher (P < 0.001), laparotomy was more commonly performed (P < 0.001), vascular tumor thrombus was more frequent (P = 0.002), CEA positive was more frequent (P < 0.001), and the likelihood of adjuvant chemotherapy was lower (P < 0.001). No significant differences were observed in gender, nerve invasion, pT stage, pN stage, CA199, CA125, and AFP levels (Table S1).

Distribution of chemotherapy regimens

Adjuvant chemotherapy, defined as chemotherapy performed after surgical resection, each regimen administered according to NCCN guidelines and administered for at least 4 cycles. We identified the following 10 adjuvant chemotherapy types for analysis (Table S2): S-1, CAPE, Paclitaxel, SOX, TS, TP, TX, PS, FOLFOX and XELOX. These included three single-agent regimens and seven combination regimens. Among the 2845 patients with adjuvant chemotherapy, 482 (16.9%) were treated with monotherapy and 2364 (83.1%) were treated with combination therapy, with SOX being the most prevalent regimen (n = 1789, 62.9%), followed by S-1 as a single-agent chemotherapy. Elderly patients were most frequently treated with S-1 monotherapy (53.7%), while younger patients underwent approximately twice the number of combination chemotherapy treatments as their elderly counterparts (84% vs 43.3%).

Survival analysis: age and adjuvant chemotherapy are independent risk factors for OS

Cox proportional hazards regression was employed to analyze the impact of various clinicopathological factors on OS and

CSS in GC patients. In the local cohort, sex, age, BMI, tumor differentiation status, pathological type, nerve invasion, vascular cancer thrombus, pT3/T4 stage, pN stage, surgical method, CEA, CA19-9, CA125 level and adjuvant chemotherapy were independent risk factors for OS. Age, pathological type, nerve invasion, pT stage, pN stage, surgical method, CEA, CA19-9, and CA125 levels were independent risk factors for CSS (Table 1). Figure 2 presents a meta-analysis forest plot to study the impact of various clinicopathological factors on OS and CSS in GC patients. In the Fujian cohort, age, pN stage, and adjuvant chemotherapy remained independent risk factors for OS (Table S3).

Kaplan–Meier curve analysis was performed for all patients. In the unadjusted analysis, the younger group had a statistically significant impact on survival when compared to the older group, and the postoperative chemotherapy group exhibited a statistically significant impact on survival when compared to the group that did not receive postoperative chemotherapy.

Patients in the elderly group had a worse prognosis, in the local cohort, the OS rates for the elderly group were 80.1%, 51.5% and 36.8% at 1, 3 and 5 years, respectively, while the OS rates for the young group were 87.1%, 64.1% and 36.8% at 1, 3 and 5 years, respectively ($P < 0.001$) (Fig. 3a). Similarly, CSS was evaluated, and in the local cohort, the CSS rates at 1, 3, and 5 years were 86.6%, 61.5, and 51% for the older group, respectively, while 92.6%, 77.2, and 71.3% at 1, 3, and 5 years for the younger group, respectively ($P < 0.001$) (Fig. 3b). In the Fujian cohort, the OS rates at 1, 3, and 5 years were 86.2%, 69.6%, and 62.6% for the older group, while the OS rates at 1, 3, and 5 years for the younger group were 99.5%, 82.5%, and 64%, respectively ($P = 0.032$) (Fig. 3c).

Patients without adjuvant chemotherapy had a worse prognosis, in the local cohort, the 1-year, 3-year, and 5-year OS rates for the group without adjuvant chemotherapy were 81.7%, 58.4%, and 49.2%, respectively, while the 1-year, 3-year, and 5-year OS rates for the group with adjuvant chemotherapy were 90%, 64.1%, and 90.9%, respectively ($P < 0.001$) (Fig. 3d). Similarly, CSS was evaluated, in the local cohort, the CSS rates at 1, 3, and 5 years were 88.5%, 72.2%, and 66.3%, respectively, whereas those who did receive adjuvant chemotherapy had OS rates of 90%, 64.1%, and 90.9% at the same time points ($P < 0.001$) (Fig. 3e). In the Fujian cohort, the 1-, 3-, and 5-year OS rates for the adjuvant chemotherapy group were 97.5%, 71.5%, and 57.5%, respectively, while those for the group without adjuvant chemotherapy were 97.5%, 71.5%, and 57.5% ($P = 0.009$) (Fig. 3f).

Stratified analysis by chemotherapy: no survival advantage from adjuvant chemotherapy in elderly patients with stage II/III gastric cancer

We believe that adjuvant chemotherapy in elderly GC patients should be evaluated more carefully. Therefore, we performed a chemotherapy stratification analysis in GC patients aged 75 years and older within both the local and Fujian cohorts. As shown in Fig. 4, in the local cohort, a statistically significant difference was observed in OS (Fig. 4a, $P < 0.001$) and CSS (Fig. 4b, $P = 0.007$) between chemotherapy and non-chemotherapy patients in the young group, Conversely, no statistically significant differences were found in OS (Fig. 4d, $P = 0.47$) and CSS (Fig. 4e, $P = 0.98$) between chemotherapy and non-chemotherapy patients in the elderly group. Similarly, in the Fujian cohort, there was a statistically significant difference in OS (Fig. 4c, $P = 0.039$) between chemotherapy and non-chemotherapy patients in the young group, whereas no statistically significant difference was observed in OS (Fig. 4f, $P = 0.482$) between chemotherapy and non-chemotherapy patients in the elderly group.

Subsequently, to account for stage-related effects, we further categorized all GC patients into stage II and stage III groups, respectively, and performed chemotherapy stratification analysis in the local cohort. As shown in Fig S1, for both stage II and stage III GC patients, there were statistically significant differences in OS (Fig S1a, $P = 0.001$; Fig S1c, $P < 0.001$) between chemotherapy and non-chemotherapy patients in the younger group, whereas no statistically significant differences in the elderly group (Fig S1b, $P = 0.51$; Fig S1d, $P = 0.243$), and the analysis of CSS yielded similar results (Fig S2).

Patients aged < 75 years were matched with patients aged ≥ 75 years on a propensity ratio of 2:1

In the local group, we used the *MatchIt* package within R software to conduct propensity score matching to address confounding bias, a 2:1 ratio was employed. Matched pairs were formed between patients aged < 75 years and those aged ≥ 75 years, with matching criteria including sex, BMI, tumor location, degree of differentiation, pathological type, pT stage, pN stage, nerve invasion, vascular cancer thrombus, surgical method, and tumor marker level, the clinicopathologic characteristics of the matched patient groups are presented in Table S4. Kaplan–Meier curve analysis and Cox regression analysis were performed on all patients in the post-matched local cohort. Results: Among the 1216 GC patients, OS and CSS remained poorer in the elderly group (Figure S3), and these outcomes were found to be associated with age and the receipt of adjuvant chemotherapy (Table 2). Chemotherapy stratification analysis was performed in GC patients ≥ 75 years, there were significant differences in OS (Fig. 5a, $P = 0.009$) and CSS (Fig. 5b, $P = 0.032$) between chemotherapy and non-chemotherapy patients in the younger group, while there was no significant differences in OS (Fig. 5c, $P = 0.708$) and CSS (Fig. 5d, $P = 0.593$)

Table 1 Univariate and multivariate analyses of overall survival and cancer-specific survival in the local cohort

Characteristic	Overall survival (n = 5009)				Cancer-specific survival (n = 3650)			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Gender								
Female	Reference		Reference		Reference			
Male	1.117 (1.021–1.221)	0.016	1.139 (1.036–1.253)	0.007	1.075 (0.943–1.224)	0.281		
Age								
< 75	Reference		Reference		Reference		Reference	
≥ 75	1.789 (1.592–2.009)	< 0.001	1.56 (1.369–1.777)	< 0.001	2.059 (1.733–2.446)	< 0.001	1.797 (1.479–2.184)	< 0.001
BMI								
18.5–24	Reference		Reference		Reference		Reference	
< 18.5	1.443 (1.285–1.62)	< 0.001	1.18 (1.043–1.335)	0.009	1.485 (1.247–1.768)	< 0.001	1.168 (0.969–1.408)	0.103
≥ 24	0.834 (0.757–0.919)	< 0.001	0.864 (0.781–0.957)	0.005	0.878 (0.763–1.01)	0.07	0.925 (0.798–1.072)	0.301
Location								
Upper	Reference		Reference		Reference		Reference	
Middle	1.025 (0.912–1.152)	0.677	1.068 (0.944–1.209)	0.297	0.953 (0.802–1.134)	0.588	0.827 (0.518–1.32)	0.426
Lower	0.922 (0.832–1.022)	0.124	0.936 (0.838–1.046)	0.243	0.878 (0.755–1.021)	0.092	0.833 (0.527–1.316)	0.434
Overlapped	2.113 (1.547–2.885)	< 0.001	1.273 (0.917–1.767)	0.15	2.16 (1.382–3.377)	0.001	0.735 (0.469–1.153)	0.18
Histology								
Adenocarcinoma	Reference		Reference		Reference		Reference	
Signet ring cell carcinoma	1.339 (1.208–1.483)	< 0.001	1.169 (1.045–1.309)	0.007	1.582 (1.367–1.83)	< 0.001	1.363 (1.16–1.6)	< 0.001
Grade								
Well	Reference		Reference		Reference		Reference	
Moderately	1.206 (1.065–1.365)	0.003	1.026 (0.897–1.173)	0.711	1.357 (1.122–1.641)	0.002	0.83 (0.676–1.018)	0.074
Poorly and undifferentiated	1.399 (1.248–1.57)	< 0.001	1.144 (1.002–1.305)	0.046	1.591 (1.333–1.899)	< 0.001	0.954 (0.826–1.1)	0.516
Nerve invasion								
No	Reference		Reference		Reference		Reference	
Yes	1.742 (1.594–1.903)	< 0.001	1.292 (1.168–1.429)	< 0.001	1.854 (1.627–2.113)	< 0.001	1.287 (1.108–1.493)	0.001
Vascular tumor thrombus								
No	Reference		Reference		Reference		Reference	
Yes	1.666 (1.535–1.808)	< 0.001	1.142 (1.041–1.253)	0.005	1.733 (1.536–1.956)	< 0.001	1.137 (0.99–1.305)	0.069
T stage								
T1	Reference		Reference		Reference		Reference	
T2	1.236 (0.846–1.804)	0.273	1.352 (0.91–2.008)	0.135	1.262 (0.715–2.229)	0.423	0.295 (0.172–0.506)	< 0.001
T3	1.931 (1.345–2.772)	< 0.001	1.915 (1.305–2.81)	0.001	1.998 (1.161–3.44)	0.012	0.428 (0.312–0.586)	< 0.001
T4	3.253 (2.34–4.522)	< 0.001	2.731 (1.921–3.882)	< 0.001	3.868 (2.36–6.338)	< 0.001	0.609 (0.473–0.785)	< 0.001
N stage								

Table 1 (continued)

Characteristic	Overall survival (n = 5009)				Cancer-specific survival (n = 3650)			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
N0	Reference		Reference		Reference		Reference	
N1	1.285 (1.089–1.517)	0.003	1.426 (1.196–1.701)	< 0.001	1.383 (1.081–1.768)	0.01	1.57 (1.207–2.043)	0.01
N2	1.879 (1.62–2.18)	< 0.001	2.022 (1.718–2.38)	< 0.001	1.993 (1.594–2.49)	< 0.001	2.159 (1.688–2.762)	< 0.001
N3	3.686 (3.211–4.231)	< 0.001	3.464 (2.955–4.061)	< 0.001	4.471 (3.639–5.493)	< 0.001	4.171 (3.286–5.293)	< 0.001
Surgery								
Open	Reference		Reference		Reference		Reference	
Laparoscope	0.697 (0.608–0.8)	< 0.001	0.831 (0.72–0.959)	0.012	0.523 (0.418–0.653)	< 0.001	0.643 (0.509–0.813)	< 0.001
CEA								
Negative	Reference		Reference		Reference		Reference	
Positive	1.562 (1.432–1.704)	< 0.001	1.319 (1.198–1.451)	< 0.001	1.623 (1.426–1.847)	< 0.001	1.353 (1.171–1.563)	< 0.001
CA199								
Negative	Reference		Reference		Reference		Reference	
Positive	1.65 (1.51–1.803)	< 0.001	1.295 (1.179–1.421)	< 0.001	1.724 (1.511–1.966)	< 0.001	1.301 (1.131–1.496)	< 0.001
CA125								
Negative	Reference		Reference		Reference		Reference	
Positive	1.76 (1.536–2.017)	< 0.001	1.636 (1.416–1.89)	< 0.001	1.806 (1.477–2.208)	< 0.001	1.74 (1.405–2.155)	< 0.001
AFP								
Negative	Reference				Reference			
Positive	1.14 (0.979–1.328)	0.092			1.114 (0.885–1.402)	0.358		
Chemotherapy								
No	Reference		Reference		Reference		Reference	
Yes	0.757 (0.7–0.819)	< 0.001	0.704 (0.645–0.769	< 0.001	0.765 (0.681–0.86)	< 0.001	0.703 (0.616–0.801)	< 0.001

between chemotherapy and non-chemotherapy patients in the elderly group.

Discussion

In 2020, the incidence of GC in China ranked third among malignant tumors, with 479,000 new cases (Cao et al. 2021; Rupaimoole et al. 2016). With the rapid development of population aging (Xia et al. 2022), GC is more prevalent among the elderly, with more than 60% of GC cases occur in patients over 65 years of age, and about one-third of GC patients over the age of 75, according to the Surveillance, Epidemiology and Final Results (SEER) database (Sung et al. 2021).

Adjuvant chemotherapy is suitable for patients with pathological stage II/III disease following D2 radical gastrectomy, and the guidelines recommend a two-drug combination regimen of fluorouracil drugs combined with platinum. For stage II gastric cancer, XELOX is the priority recommendation. For those with poor physical condition, advanced age, and intolerance to the two-drug combination regimen, S-1 monotherapy with oral fluorouracil drugs should be actively considered, and XP, SOX, and FLOFOX regimens can also be considered (Park et al. 2021; Zhang et al. 2021). For stage III patients, XELOX (Bang et al. 2012) and SOX (Cheng et al. 2021) regimens are preferentially recommended. The results of the S-1 gastric cancer adjuvant chemotherapy trial (ACTS-GC) (Sasako et al. 2011) showed that: the 5-year OS was significantly improved by 10.6% (71.7 vs. 61.1%, HR 0.669,

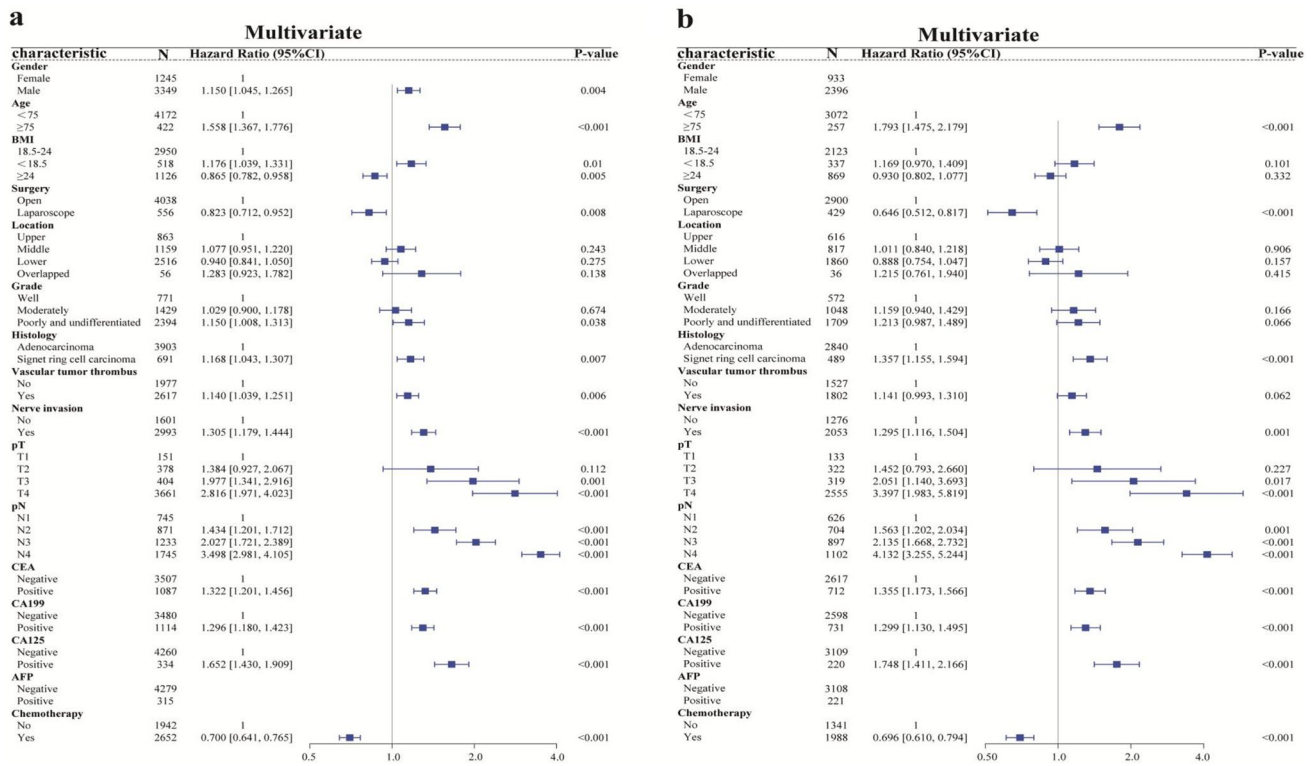

Fig. 2 **a** Forest plot of independent prognostic factors for overall survival in gastric cancer postoperative chemotherapy. **b** Forest plot of core hazard ratios for cancer-specific survival in gastric cancer postoperative chemotherapy

95% CI: 0.540–0.828) and 5-year RFS improved by 12.3% (65.4 vs. 53.1%, HR 0.653, 95% CI: 0.537–0.793) in the adjuvant S-1 chemotherapy group compared with surgery alone Based on this study, S-1 was established as the standard of postoperative adjuvant chemotherapy for patients undergoing radical surgery for locally advanced gastric cancer in East Asia. The adjuvant study of capecitabine and oxaliplatin in gastric cancer (CLASSIC) (Bang et al. 2012) was a phase III study conducted in East Asia, This study reported the significant efficacy of DFS after 6 months of adjuvant treatment (postoperatively) with capecitabine plus oxaliplatin (XELOX) after gastrectomy with D2 lymph node dissection compared to surgery alone. However, these clinical trials do not adequately represent elderly patients, frail patients, and especially frail elderly patients. Most of the current clinical studies limit enrollment to patients under 75 years, unreasonably excluding elderly subjects from clinical trials, leading to an unrepresentative study population. This, in turn, presents challenges in applying study findings to the target population (Pitkala and Strandberg 2022; Thake and Lowry 2017). Clinicians often treat older cancer patients according to guidelines developed for the general population, which can be risky for these patients who may have multiple comorbidities (Aapro et al. 2005).

Previously, some researchers have explored to help elderly and frail cancer patients develop appropriate chemotherapy regimens. In 2011, Seymour et al. (2011) conducted the nationwide randomized trial MRC FOCUS2 in frail and elderly patients with colorectal cancer, they used reduced doses of chemotherapy, and the two primary outcomes were: progression-free survival (PFS) and change in overall quality of life (QOL) from baseline to 12 weeks, the moderate rates of toxic side effects and improvements in good quality of life observed across all treatment groups supported the view that elderly and frail cancer patients may not benefit from full-dose chemotherapy. The GO2 (Hall et al. 2021) randomized clinical trial was the first large-scale study to investigate the association between chemotherapy intensity and patient-centric outcomes in frail and elderly cancer patients. In this trial, 514 elderly frail patients with gastroesophageal cancer received the standard XELOX regimen at an 80% dose, and the reduced-dose regimen showed reduced toxicity and comparable survival outcomes compared to those of the standard dose. 321GO (Hall et al. 2017) was a randomized phase II trial and feasibility study on palliative chemotherapy in frail or elderly patients with advanced gastroesophageal cancer, the median age of the enrolled population was 75 years, all patients were randomized in a 1:1:1 ratio to receive epirubicin, oxaliplatin, and capecitabine (EOX); oxaliplatin plus

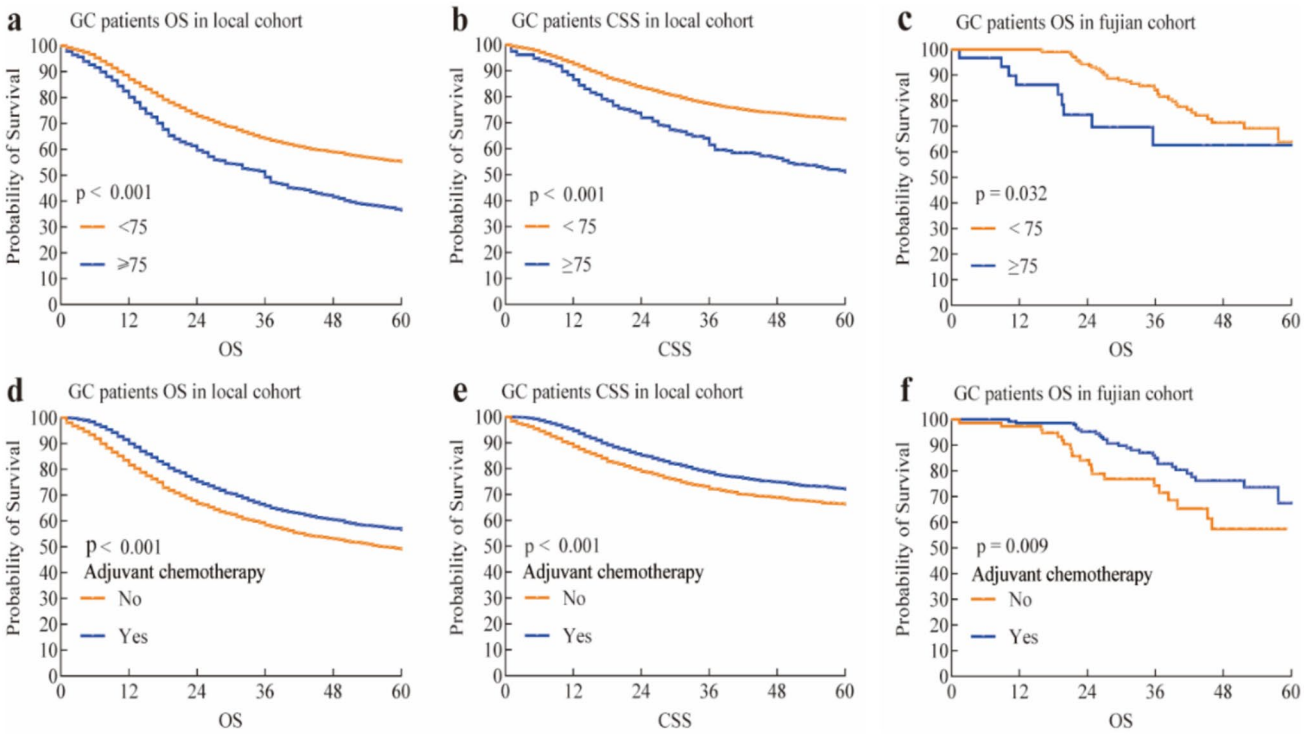

Fig. 3 OS and CSS in GC patients with stage II and III. **a** OS for patients aged < 75 and ≥ 75 years in local cohort. **b** CSS for patients aged < 75 and ≥ 75 years in local cohort. **c** OS for patients aged < 75 and ≥ 75 years in fujian cohort. **d** OS for patients with or without adjuvant chemotherapy in local cohort. **e** CSS for patients with or without adjuvant chemotherapy in local cohort. **f** OS for patients with or without adjuvant chemotherapy in fujian cohort

capecitabine (OX); Single-agent capecitabine (X) (80% of the full dose), and finally, the patient's overall quality of life improved with treatment. These trials have demonstrated that standard clinical trial-based guidelines are not directly applicable to the treatment of elderly cancer patients.

Currently, there is no universally agreed-upon age cutoff for defining"elderly patients", and the International Cancer Society differing on this definition. The European Society of Medical Oncology (ESMO) defines elderly as patients aged 70 years or older, while the American Society of Clinical Oncology (ASCO) defines patients ≥ 65 years of age as elderly (Mohile et al. 2018), reflecting differences in life expectancy around the world. A previous study in China enrolled 5,762 GC patients, determined an optimal age cutoff of 75 years for elderly gastric cancer using a k-adaptive partition algorithm. Subsequently, this study classified patients into young and elderly groups based on an age threshold of 75 years, baseline characteristics showed that compared with the young group, the elderly group exhibited a lower BMI, a higher degree of tumor differentiation, a lower prevalence of signet ring cell carcinoma, and a lower likelihood of receiving adjuvant chemotherapy, aligning with findings from previous studies. Guo et al. (2023) analyzed 283 GC patients with stage II/III, concluded that elderly patients exhibited a lower BMI (P < 0.001), a higher degree of tumor differentiation (P = 0.017), and a reduced likelihood of receiving adjuvant chemotherapy (P < 0.001). A study by Hogan et al. (2020) reported that poorly differentiated GC, especially signet ring cell carcinoma, was less common in elderly GC patients compared to young patients, whereas high/moderately differentiated gastric cancer was more frequent in elderly patients. The lower proportion of elderly cancer patients receiving adjuvant chemotherapy may be due to the shorter life expectancy, a higher incidence of comorbidities, higher risk of complications, and the reluctance of the elderly to undergo adjuvant chemotherapy (Kawaguchi et al. 2021). Furthermore, this study also found that elderly patients were more likely to undergo open surgery than laparoscopic surgery (93.2% vs 6.8%), and elderly patients were more likely to undergo laparotomy compared to younger patients (93.25% vs 87%). We suspect that this may be related to the fact that laparoscopic surgery for advanced gastric cancer is still considered by most scholars to be cautious, large-scale prospective randomized controlled studies JCOG0912 (Katai et al. 2020) and KLASS-01 (Kim et al. 2019) have both confirmed that laparoscopic surgery for distal gastrectomy in cT1 N0 and cT1 N1 gastric cancer is as safe as laparotomy and does not significantly impact long-term prognosis, these findings support the use of laparoscopic surgery as a standard treatment

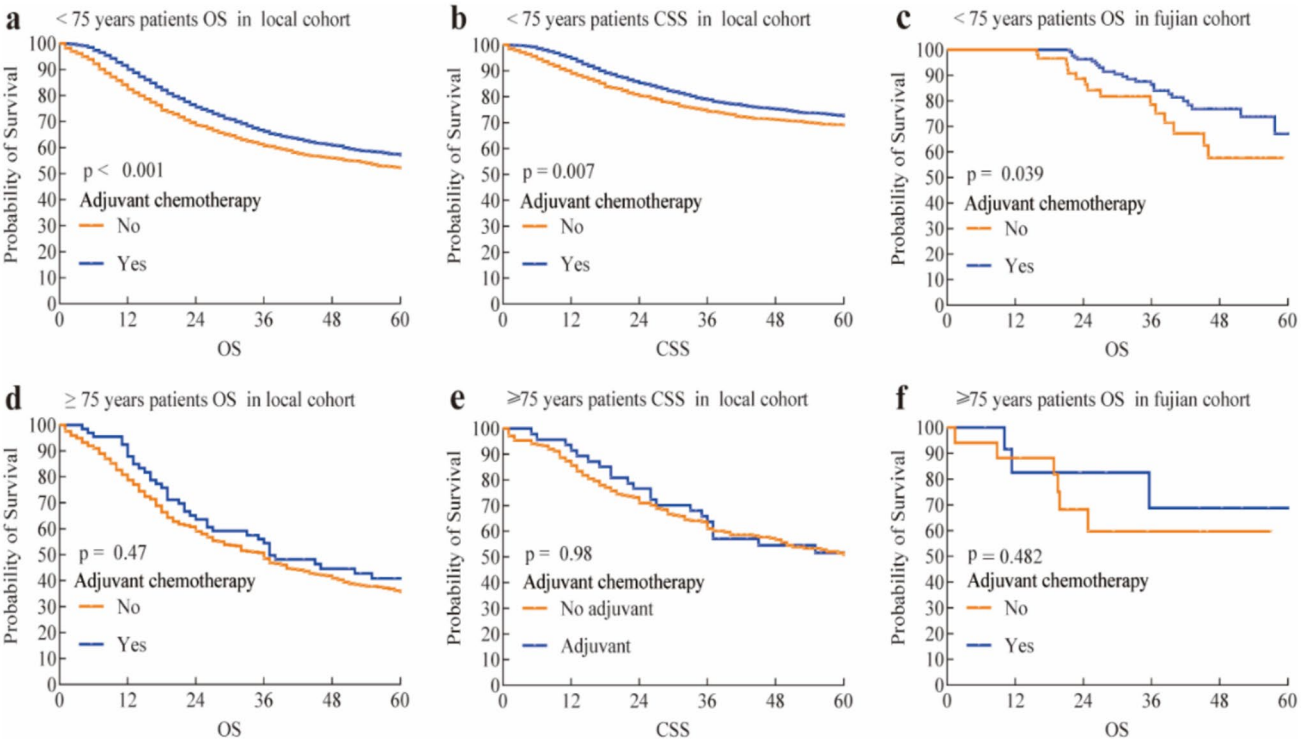

Fig. 4 OS (**a**) and CSS (**b**) with or without adjuvant chemotherapy in patients < 75 years of age in local cohort; **c** OS with or without adjuvant chemotherapy in patients < 75 years of age in fujian cohort; OS (**d**) and CSS (**e**) with or without adjuvant chemotherapy in patients ≥ 75 years of age in local cohort; **f** OS with or without adjuvant chemotherapy in patients ≥ 75 years of age in fujian cohort

for early distal gastric cancer, while for advanced gastric cancer, further clinical research is warranted.

Whether adjuvant chemotherapy confers a survival advantage in elderly gastric cancer patients with stage II/III disease remains controversial in some prior studies and publications. The results of a study based on 404 elderly GC patients with stage II/III by Shi et al. (2023) showed that, compared to those who did not receive adjuvant chemotherapy, the survival of younger patients who did was better than that of elderly patients ($P < 0.001$), adjuvant chemotherapy significantly improved disease-free survival (DFS) (5-year DFS rate, 53.1% vs 30.4%, $P < 0.001$) and overall survival (OS) (5-year OS rate, 68.7% vs 52.1%; $P = 0.002$). These findings suggest that adjuvant chemotherapy may offer benefits to elderly patients with stage II/III gastric cancer aged ≥ 70 years. A cohort study based on GC patients by Cheng (2023) et al. concluded that adjuvant chemotherapy was associated with better OS compared to surgery-only, adjuvant chemotherapy significantly improved OS and CSS in elderly patients with stage II/III GC. Karaca et al. (2018) found that adjuvant chemotherapy in elderly GC patients is as effective as in non-elderly patients, based on a comparison of survival rates between elderly and young GC patients receiving adjuvant chemotherapy. In contrast, a multicenter study by Guo et al. (2023) found inconsistent results, indicating that adjuvant chemotherapy may not be beneficial for elderly gastric cancer patients with stage II/III disease. Recently, Noguez-Ramos et al. (2024) conducted a systematic review and meta-analysis of 7 previous clinical trials and find that chemotherapy did not significantly improve OS or RFS compared to surgery alone or de-escalation chemotherapy in the treatment of patients with gastroesophageal adenocarcinoma aged 70 years or older.

In this study, Kaplan–Meier curve analysis was performed on all patients in both cohorts, revealing that the elderly group had poorer OS and CSS compared to the younger group. Stratified analysis of chemotherapy in gastric cancer patients over 75 years revealed a statistically significant difference in OS and CSS between the chemotherapy and non-chemotherapy groups among younger patients, whereas no such difference was observed in the elderly group (Fig. 4). Subsequently, to reduce confounding bias, we matched propensity scores for all patients in the local cohort (Austin et al. 2018; Liang et al. 2021), and the results showed that there was a statistically significant difference in OS and CSS between the chemotherapy and non-chemotherapy groups in the younger group, while there was no significant difference in OS and CSS between the chemotherapy and non-chemotherapy groups in the older group (Fig. 5). Consequently, this study's findings indicate that adjuvant chemotherapy

Table 2 Univariate and multivariate analyses of overall survival and cancer-specific survival in the local cohort after PSM

Characteristic	Overall survival (n = 1216)				Cancer-specific survival (n = 828)			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
Gender								
Female	Reference		Reference		Reference			
Male	1.232 (1.035, 1.467)	0.019	1.293 (1.082, 1.544)	0.005	1.240 (0.957, 1.606)	0.104		
Age								
< 75	Reference		Reference		Reference		Reference	
≥ 75	1.646 (1.416, 1.913)	< 0.001	1.469 (1.238, 1.744)	< 0.001	1.844 (1.473, 2.307)	< 0.001	1.635 (1.270, 2.103)	< 0.001
BMI								
18.5–24	Reference		Reference		Reference		Reference	
< 18.5	1.377 (1.137, 1.667)	0.001	1.156 (0.949, 1.407)	0.15	1.464 (1.102, 1.945)	0.008	1.223 (0.912, 1.641)	0.178
≥ 24	0.829 (0.682, 1.009)	0.062	0.832 (0.682, 1.015)	0.07	0.894 (0.671, 1.192)	0.446	0.928 (0.692, 1.244)	0.615
Surgery								
Open	Reference				Reference			
Laparoscope	0.832 (0.609, 1.137)	0.248			0.873 (0.566, 1.348)	0.541		
Location								
Upper	Reference		Reference		Reference		Reference	
Middle	0.869 (0.695, 1.087)	0.219	0.775 (0.617, 0.974)	0.029	0.683 (0.484, 0.965)	0.030	0.576 (0.405, 0.820)	0.002
Lower	0.859 (0.721, 1.023)	0.088	0.820 (0.684, 0.983)	0.032	0.754 (0.586, 0.969)	0.028	0.643 (0.495, 0.835)	0.001
Overlapped	2.025 (1.153, 3.556)	0.014	1.159 (0.645, 2.082)	0.621	1.944 (0.901, 4.196)	0.090	0.951 (0.423, 2.141)	0.904
Grade								
Well	Reference		Reference		Reference		Reference	
Moderately	1.239 (0.997, 1.541)	0.053	1.006 (0.801, 1.265)	0.958	1.387 (0.995, 1.933)	0.053	1.115 (0.786, 1.581)	0.542
Poorly and undifferentiated	1.668 (1.358, 2.048)	< 0.001	1.224 (0.973, 1.538)	0.084	1.937 (1.417, 2.648)	< 0.001	1.323 (0.932, 1.878)	0.118
Histology								
Adenocarcinoma	Reference		Reference		Reference		Reference	
Signet ring cell carcinoma	1.816 (1.470, 2.243)	< 0.001	1.433 (1.143, 1.797)	0.002	2.408 (1.795, 3.230)	< 0.001	1.753 (1.278, 2.405)	0.001
Vascular tumor thrombus								
No	Reference		Reference		Reference		Reference	
Yes	1.683 (1.433, 1.975)	< 0.001	1.158 (0.965, 1.389)	0.115	1.810 (1.426, 2.299)	< 0.001	1.192 (0.910, 1.563)	0.202
Nerve invasion								
No	Reference		Reference		Reference		Reference	
Yes	1.795 (1.522, 2.116)	< 0.001	1.283 (1.068, 1.540)	0.008	1.972 (1.542, 2.521)	< 0.001	1.485 (1.142, 1.930)	0.003
T stage								
T1	Reference		Reference		Reference			
T2	1.034 (0.474, 2.257)	0.932	1.060 (0.480, 2.338)	0.886	0.847 (0.273, 2.628)	0.774		

Table 2 (continued)

Characteristic	Overall survival (n = 1216)				Cancer-specific survival (n = 828)			
	Univariate		Multivariate		Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value	HR (95% CI)	P-value
T3	1.516 (0.718, 3.201)	0.276	1.364 (0.636, 2.924)	0.426	1.296 (0.443, 3.793)	0.636		
T4	2.335 (1.163, 4.691)	0.017	1.850 (0.903, 3.791)	0.093	2.380 (0.887, 6.387)	0.085		
N stage								
N0	Reference		Reference		Reference		Reference	
N1	1.125 (0.825, 1.534)	0.455	1.316 (0.957, 1.810)	0.091	1.099 (0.691, 1.747)	0.691	1.153 (0.720, 1.847)	0.554
N2	2.037 (1.563, 2.654)	< 0.001	2.126 (1.598, 2.829)	< 0.001	2.311 (1.564, 3.417)	< 0.001	2.132 (1.405, 3.235)	< 0.001
N3	3.622 (2.800, 4.685)	< 0.001	3.130 (2.328, 4.208)	< 0.001	4.165 (2.849, 6.089)	< 0.001	3.255 (2.109, 5.026)	< 0.001
CEA								
Negative	Reference		Reference		Reference		Reference	
Positive	1.483 (1.263, 1.741)	< 0.001	1.371 (1.157, 1.624)	< 0.001	1.568 (1.233, 1.994)	< 0.001	1.445 (1.121, 1.862)	0.004
CA199								
Negative	Reference		Reference		Reference		Reference	
Positive	1.256 (1.068, 1.477)	0.006	1.058 (0.894, 1.253)	0.51	1.278 (1.005, 1.626)	0.046	1.066 (0.832, 1.367)	0.612
CA125								
Negative	Reference		Reference		Reference		Reference	
Positive	1.980 (1.538, 2.548)	< 0.001	1.783 (1.378, 2.308)	< 0.001	2.063 (1.431, 2.973)	< 0.001	1.861 (1.275, 2.715)	0.001
AFP								
Negative	Reference				Reference			
Positive	0.849 (0.626, 1.152)	0.294			0.733 (0.456, 1.180)	0.201		
Chemotherap								
No	Reference		Reference		Reference		Reference	
Yes	0.677 (0.583, 0.787)	< 0.001	0.694 (0.582, 0.827)	< 0.001	0.659 (0.527, 0.823)	< 0.001	0.661 (0.512, 0.853)	0.001

does not confer a survival advantage to elderly gastric cancer patients with stage II/III disease.

We analyzed that this may be attributed to the relative homogeneity of health in younger cancer patients. Variations in organ function, pharmacokinetics, gastrointestinal absorption, and metabolism between younger and older patients, as well as among the elderly, may result in significant disparities in the effectiveness and safety of cancer therapies (Reid-Agboola et al. 2023). Matsunaga et al. (2021) argue that older patients are more susceptible to comorbidities, including hypertension, coronary heart disease, and diabetes, compared to younger patients. They also tend to have poorer nutritional status and inflammation levels. Consequently, traditional chemotherapy regimens may pose more harm than benefit for this population. We advise a comprehensive evaluation of postoperative adjuvant chemotherapy for gastric cancer patients aged 75 and older. Identifying frail and vulnerable elderly patients remains a challenge. CGA is a validated score that can help patients stratify when making clinical decisions, however, although ESMO recommends the use of CGA at the onset of treatment in elderly patients with gastroesophageal adenocarcinoma, the tolerance to chemotherapy has not been systematically evaluated using standardized approaches (Lordick et al. 2022). The FOCUS2 study pioneered the use of Overall Treatment Utility (OTU) as a patient-centered method to evaluate the benefits of cancer treatment. OTU integrates clinical efficacy, tolerability, and the patient's subjective assessment of treatment value. In this trial, OTU highlighted the distinct advantages of oxaliplatin chemotherapy for elderly and frail patients with advanced colorectal cancer, even when other conventional endpoints showed variability. However,

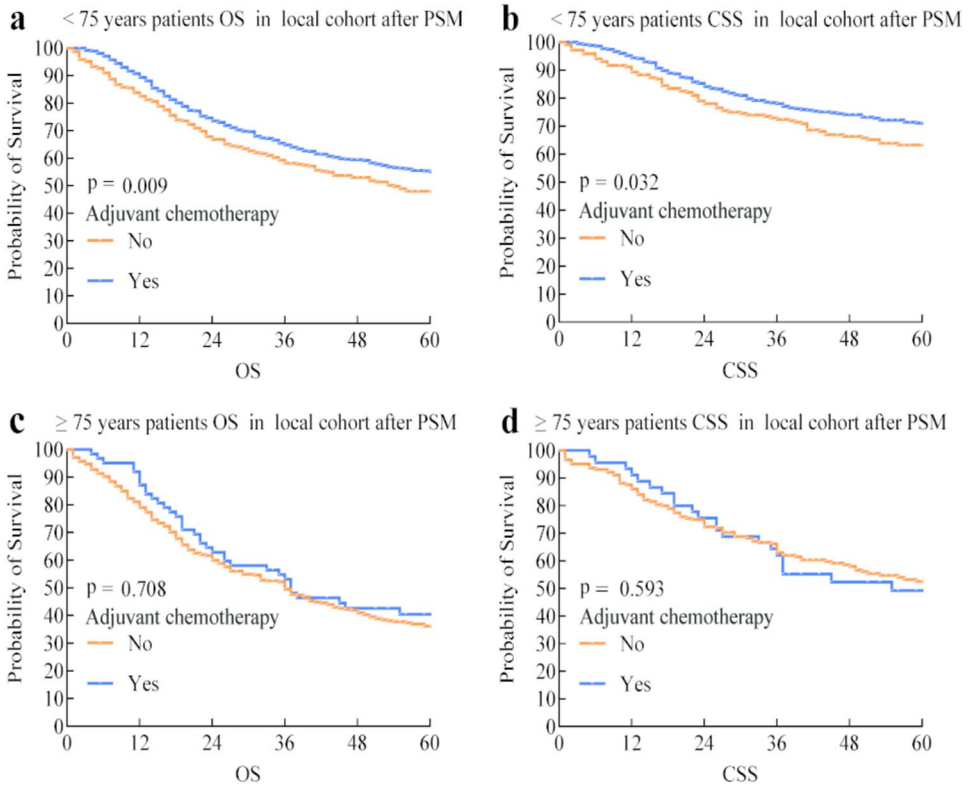

Fig. 5 OS and CSS with or without adjuvant chemotherapy in patients aged < 75 (**a**, **b**) and ≥ 75 (**c**, **d**) years of age in local cohort after PSM

there is still no definitive evaluation criterion for identifying frail elderly cancer patients and assessing the benefits of chemotherapy.

We look forward to more clinical researches on elderly GC patients in the future, to further investigate the effects of adjuvant chemotherapy on their survival, establish criteria for identifying and assessing the benefits of chemotherapy in frail and elderly patients, identify chemotherapy regimens with minimal toxicity for advanced-stage elderly and frail patients, and offer additional treatment options for both clinicians and cancer patients. This study's strengths include the use of propensity score matching to minimize confounding bias. Conducted as a multicenter cohort study, it enrolled GC patients from Zhejiang Cancer Hospital and Fujian Cancer Hospital, thereby mitigating the influence of regional variables and reducing selection bias. This study also has several limitations. First, this study is a retrospective design, selection bias is inevitable, it is important to note that healthier older patients may be given preference to chemotherapy, and the observational retrospective design itself limits causal inference, as treatment allocation is non-random, and while propensity score matching can help control for confounding bias, it can lead to smaller sample sizes and unbalanced covariates. Second, this study only pooled all adjuvant regimens (monotherapy versus combination therapy) and did not further distinguish the effect of different chemotherapy regimens on adjuvant chemotherapy, as the primary aim was to assess the association of adjuvant chemotherapy with survival outcomes, regardless of specific treatment regimens, and all participating centers were tertiary hospitals in East Asia, where GC biology and treatment paradigms differed compared to Western populations, These factors limit external validity and therefore additional research is required to elucidate these differences.

Conclusions

In this multicenter study, we found that age and adjuvant chemotherapy were independent risk factors for OS and CSS in GC patients with stage II/III; Adjuvant chemotherapy may not confer a survival benefit in older patients with stage II/III gastric cancer. These findings offer a valuable reference for clinicians in developing rational and optimal treatment plans for elderly GC patients, for stage II/III gastric cancer patients aged ≥ 75 years, our data support shared decision-making with careful consideration of functional status and comorbidities, rather than routine administration of adjuvant chemotherapy.

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Availability of data and materials No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical approval and consent to participate This study was undertaken in accordance with the World Medical Association-Declaration of Helsinki- ethical principles for medical research, and was designed as a single-center, retrospective study approved by the Medical Ethics Committee of Zhejiang Cancer Hospital (IRB-2022-371). All patients gave their informed consent.

Consent for publication Not applicable.

References

Aapro MS, Kohne CH, Cohen HJ et al (2005) Never too old? Age should not be a barrier to enrollment in cancer clinical trials. Oncologist 10(3):198–204

Austin PC, Jembere N, Chiu M (2018) Propensity score matching and complex surveys. Stat Methods Med Res 27(4):1240–1257

Bang YJ, Kim YW, Yang HK et al (2012) Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial. Lancet 379(9813):315–321

Cao W, Chen HD, Yu YW et al (2021) Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. Chin Med J (Engl) 134(7):783–791

Chan WL, Liu X, Wong CK et al (2023) Adjuvant chemotherapy in older patients with gastric cancer: a population-based cohort study. Cancers (Basel) 15(15):3768

Chen W, Zheng R, Baade PD et al (2016) Cancer statistics in China, 2015. CA Cancer J Clin 66(2):115–132

Cheng X, Wu D, Xu N et al (2021) Adjuvant albumin-bound paclitaxel combined with S-1 vs oxaliplatin combined with capecitabine after D2 gastrectomy in patients with stage III gastric adenocarcinoma: a phase III multicenter, open-label, randomized controlled clinical trial protocol. BMC Cancer 21(1):56

Guo J, Xiong Z, Yin S et al (2023) Elderly patients with stage II gastric cancer do not benefit from adjuvant chemotherapy. World J Surg Oncol 21(1):319

Hall PS, Lord SR, Collinson M et al (2017) A randomised phase II trial and feasibility study of palliative chemotherapy in frail or elderly patients with advanced gastroesophageal cancer (321GO). Br J Cancer 116(4):472–478

Hall PS, Swinson D, Cairns DA et al (2021) Efficacy of reduced-intensity chemotherapy with oxaliplatin and capecitabine on quality of life and cancer control among older and frail patients with advanced gastroesophageal cancer: the GO2 phase 3 randomized clinical trial. JAMA Oncol 7(6):869–877

Joharatnam-Hogan N, Shiu KK, Khan K (2020) Challenges in the treatment of gastric cancer in the older patient. Cancer Treat Rev 85:101980

Ju W, Zheng R, Zhang S et al (2023) Cancer statistics in Chinese older people, 2022: current burden, time trends, and comparisons with the US, Japan, and the Republic of Korea. Sci China Life Sci 66(5):1079–1091

Karaca M, Tural D, Kocoglu H et al (2018) Adjuvant chemotherapy for gastric cancer in elderly patients has same benefits as in younger patients. J Cancer Res Ther 14(3):593–596

Katai H, Mizusawa J, Katayama H et al (2020) Survival outcomes after laparoscopy-assisted distal gastrectomy versus open distal gastrectomy with nodal dissection for clinical stage IA or IB gastric cancer (JCOG0912): a multicentre, non-inferiority, phase 3 randomised controlled trial. Lancet Gastroenterol Hepatol 5(2):142–151

Kawaguchi Y, Akaike H, Shoda K et al (2021) Is surgery the best treatment for elderly gastric cancer patients? World J Gastrointest Surg 13(11):1351–1360

Kim HH, Han SU, Kim MC et al (2019) Effect of laparoscopic distal gastrectomy vs open distal gastrectomy on long-term survival among patients with stage I gastric cancer: the KLASS-01 randomized clinical trial. JAMA Oncol 5(4):506–513

Liang J, Hu Z, Zhan C et al (2021) Using propensity score matching to balance the baseline characteristics. J Thorac Oncol 16(6):e45–e46

Lordick F, Carneiro F, Cascinu S et al (2022) Gastric cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up. Ann Oncol 33(10):1005–1020

Matsunaga T, Ishiguro R, Miyauchi W et al (2021) Appraisal of long-time outcomes after curative surgery in elderly patients with gastric cancer: a propensity score matching analysis. BMC Surg 21(1):33

Mohile SG, Dale W, Somerfield MR et al (2018) Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric Oncology. J Clin Oncol 36(22):2326–2347

Noguez-Ramos A, Gervaso L, Catanese S et al (2024) Efficacy and safety of systemic chemotherapy for radically resectable esophago-gastric adenocarcinoma in older patients: a systematic review and meta-analysis. J Geriatr Oncol 15(1):101600

Noh SH, Park SR, Yang HK et al (2014) Adjuvant capecitabine plus oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): 5-year follow-up of an open-label, randomised phase 3 trial. Lancet Oncol 15(12):1389–1396

Park SH, Lim DH, Sohn TS et al (2021) A randomized phase III trial comparing adjuvant single-agent S1, S-1 with oxaliplatin, and postoperative chemoradiation with S-1 and oxaliplatin in patients with node-positive gastric cancer after D2 resection: the ARTIST 2 trial(☆). Ann Oncol 32(3):368–374

Pitkala KH, Strandberg TE (2022) Clinical trials in older people. Age Ageing. https://doi.org/10.1093/ageing/afab282

Reid-Agboola C, Klukowska A, Malcolm FL et al (2023) Comprehensive geriatric assessment for older women with early-stage (non-metastatic) breast cancer-an updated systematic review of the literature. Curr Oncol 30(9):8294–8309

Rupaimoole R, Calin GA, Lopez-Berestein G et al (2016) miRNA deregulation in cancer cells and the tumor microenvironment. Cancer Discov 6(3):235–246

Sakuramoto S, Sasako M, Yamaguchi T et al (2007) Adjuvant chemotherapy for gastric cancer with S-1, an oral fluoropyrimidine. N Engl J Med 357(18):1810–1820

Sasako M, Sakuramoto S, Katai H et al (2011) 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 29(33):4387–4393

Seymour MT, Thompson LC, Wasan HS et al (2011) Chemotherapy options in elderly and frail patients with metastatic colorectal cancer (MRC FOCUS2): an open-label, randomised factorial trial. Lancet 377(9779):1749–1759

Shih YH, Lin HC, Liao PW et al (2023) The efficacy of adjuvant chemotherapy for older adults with stage II/III gastric cancer: a retrospective cohort study. BMC Cancer 23(1):770

Sung H, Ferlay J, Siegel RL et al (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71(3):209–249

Sung H, Ferlay J, Siegel RL et al (2021) Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71(3):209–249

Takayama T, Tsuji Y (2023) Updated adjuvant chemotherapy for gastric cancer. J Clin Med 12(21):6727

Thake M, Lowry A (2017) A systematic review of trends in the selective exclusion of older participant from randomised clinical trials. Arch Gerontol Geriatr 72:99–102

Vollset SE, Goren E, Yuan CW et al (2020) Fertility, mortality, migration, and population scenarios for 195 countries and territories from 2017 to 2100: a forecasting analysis for the Global Burden of Disease Study. Lancet 396(10258):1285–1306

Xia C, Dong X, Li H et al (2022) Cancer statistics in China and United States, 2022: profiles, trends, and determinants. Chin Med J (Engl) 135(5):584–590

Yoshida K, Kodera Y, Kochi M et al (2019) Addition of docetaxel to oral fluoropyrimidine improves efficacy in patients with stage III gastric cancer: interim analysis of JACCRO GC-07, a randomized controlled trial. J Clin Oncol 37(15):1296–1304

Zhang X, Liang H, Li Z et al (2021) Perioperative or postoperative adjuvant oxaliplatin with S-1 versus adjuvant oxaliplatin with capecitabine in patients with locally advanced gastric or gastro-oesophageal junction adenocarcinoma undergoing D2 gastrectomy (RESOLVE): an open-label, superiority and non-inferiority, phase 3 randomised controlled trial. Lancet Oncol 22(8):1081–1092