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Disparities in overall survival of gastric cancer patients after radical gastrectomy: an age and rural-urban residence-based cohort study with propensity score matching analysis

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This study estimated overall survival (OS) among gastric cancer patients stratified by age and rural-urban residence after radical gastrectomy. Patients (*n* = 286) undergoing curative gastrectomy were categorized into four groups based on age (older ≥ 60 years or younger < 60 years) and residence (rural or urban), including rural older (G1), urban older (G2), rural younger (G3) and urban younger (G4) groups. G1 presented with significantly more males, upper stomach cancers and total gastrectomies, while less patients receiving ≥ 4 cycles of adjuvant chemotherapy. The 5-year OS rates were 39.9% for G1, 61.1% for G2, 73.1% for G3, and 71.2% for G4, with a median OS of 47 months in G1 and not reached for other groups. OS was significantly worse in G1 than other groups (*P* < 0.05). Multivariate Cox regression identified age, type of gastrectomy, adjuvant chemotherapy, perineural invasion, pT category and pN category as independent prognostic factors. After propensity score matching, rural older patients continued to show significantly inferior OS compared to urban older (hazard ratio = 2.269 [1.274–4.042], *P* = 0.005) and rural younger (hazard ratio = 2.103 [1.116–3.961], *P* = 0.021) patients. Rural older patients suffered poorer OS after radical gastrectomy, highlighting the need for special attention and comprehensive treatment strategies.

Keywords Gastric cancer, Older, Rural residence, Overall survival, Radical gastrectomy, Propensity score matching

In China, gastric cancer ranks third among malignant tumors in terms of both incidence and mortality, with approximately 400,000 new cases and nearly 300,000 deaths reported annually[1]. Gastric cancer has a strong relationship with geographical area, gender and age, with particularly pronounced disease burden in rural areas, males and older adults aged over 60 years old[2]. Before the implementation of a nationwide population-based gastric cancer screening program in 2012, most cases were diagnosed at middle or late stages, resulting in high mortality and a 5-year survival rate of less than 40%.[3,4]

Radical gastrectomy with adjuvant chemotherapy has been established as one of the standard treatments for gastric cancer[5]. However, data from the "China Gastrointestinal Cancer Surgery Union" indicated that the proportion of patients with early gastric cancer undergoing surgical treatment was low, with less than 20%, and even lower in southwest China, indicating potential challenges in early detection and management of gastric cancer in certain regions[6].

The prognosis of gastric cancer is influenced by a multitude of clinicopathological features including sex, age, TNM stage and treatment modalities[7–9]. Emerging evidence suggests that socioeconomic factors and living area may also play a significant role in determining outcomes for patients with gastric cancer[10,11]. In regions

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like southwest China, where economic and social development may be relatively less advanced compared to east China, there may be notable disparities in healthcare accessibility, quality of care and overall outcomes for patients with gastric cancer. Additionally, the prevalent trend of rural-to-urban migration, characterized by the movement of young and middle-aged adults to urban centers for better opportunities, leaving behind older parents in rural areas, can have implications for the care and support available to older individuals[12–14]. This situation is particularly pertinent to gastric cancer care, as the older "left behind" in rural areas might encounter difficulties in obtaining timely and appropriate healthcare services, including cancer screening, diagnosis, and treatment. The lack of social support and resources in rural areas can further exacerbate these disparities and impact the prognosis of gastric cancer patients who belong to this demographic group.

The survival outcomes of gastric cancer patients, stratified by age and rural-urban residence, especially within the context of Sichuan province, remain understudied and merit deeper exploration. The present study focused on clinicopathological features and overall survival (OS) of gastric cancer patients of Sichuan province and aimed to gain insights into the factors that may impact prognosis.

Methods

Patients selection

A retrospective analysis was conducted in consecutive patients with gastric cancer who underwent radical gastrectomy by a single surgical team from January 2013 to June 2016. This study was approved by the Institutional Review Board of Sichuan Cancer Hospital and written informed consent was waived due to its retrospective design (SCCSMC-01-2024-110). All methods were performed in accordance with relevant guidelines and regulations. The inclusion criteria were as follows: pathologically confirmed gastric or gastroesophageal junction adenocarcinoma, aged over 18 years, radical gastrectomy with D1+/D2 lymph node dissection, and with or without adjuvant chemotherapy. In this study, 5-fluorouracil or S-1 and oxaliplatin combination therapy or S-1 monotherapy was the major adjuvant therapeutic regimen. The exclusion criteria encompassed patients with distant metastases (M1), R1/R2 resection, and those lacking complete clinicopathological features or follow-up information. Patients were divided into four groups according to age at surgery (older ≥ 60 or younger < 60 years old) and residence area (rural or urban), including rural older group (G1), urban older group (G2), rural younger group (G3), and urban younger group (G4). The age cutoff of 60 years was selected based on the World Health Organization's definition of older adults and relevant legal standards in China. Rural and urban classifications were determined according to the administrative division standards of the National Bureau of Statistics of China, with rural areas defined as counties and below, and urban areas as prefecture-level cities and above.

Data collection

The study gathered demographic and clinical data from electronic medical records, encompassing various baseline characteristics such as age at surgery, sex, place of residence, duration of illness (the length of time from onset of symptoms to diagnosis of gastric cancer), comorbidities, American Society of Anesthesiologists (ASA) classification, body mass index (BMI), hemoglobin, and albumin levels. Additionally, treatment details such as perioperative blood transfusion, type of gastrectomy, and adjuvant chemotherapy were noted, along with pathological features including tumor location, size, macroscopic type, histopathological grading, lymphatic/venous invasion, perineural invasion and stage. Tumor staging adhered to the 7th edition UICC TNM Classification of Malignant Tumors[15]. Residence areas were classified as rural or urban based on the patient's registered permanent place of residence.

Patient follow-up

Follow-up was conducted by regular outpatient visits and telephone follow-ups. OS was defined as the time from surgery to death from any cause. Relapse-free survival (RFS) was defined as the time from surgery to any disease recurrence (local, regional, or distant), but death was censored (not included). The final follow-up was completed in June 2021 to allow for at least a 5-year follow-up for all patients.

Statistical analysis

The database was developed and maintained using Microsoft Excel version 2016, while SPSS version 26 was utilized for data analysis. Categorical variables were analyzed using frequency with percentage, and $\chi 2$ test was utilized for intergroup comparisons. Numerical variables were presented as median with range, and Kruskal-Wallis test was used for comparisons among multiple groups, while Mann-Whitney U test for comparisons between two groups. Bonferroni correction was performed to adjust the p-values for multiple comparisons. Survival analysis was conducted using Kaplan-Meier method with log rank test and Cox regression with forward LR method. The proportional hazards assumption of the Cox model was assessed using the Schoenfeld residual test. If the p-value was greater than 0.05, the assumption was considered to be met. Propensity score matching (PSM) was calculated using sex, age, comorbidities, ASA class, BMI, hemoglobin and albumin levels, tumor location, tumor size and macroscopic type as matching factors to balance baseline characteristics between rural and urban groups in older patients, and between older and younger groups in rural patients. Nearest neighbor matching was performed without replacement at a ratio of 1:1 and a match tolerance of 0.1. The standardized mean difference (SMD) was calculated to assess the balance of covariates between the matched groups.

Conference presentation

The results of the study were partly presented as posters in the International Gastric Cancer Congress 2022 and the 94th Annual Meeting of the Japanese Gastric Cancer Association, respectively.

Results

Patient characteristics and pathological features

A flow diagram of the patient selection is presented in Fig. 1. From 360 patients considered for eligibility, 286 patients who received curative-intent surgery with or without adjuvant chemotherapy were identified as study subjects.

The patient characteristics and pathological features are summarized in Table 1, demonstrating notable variations in sex, ASA class, BMI, albumin levels, perioperative blood transfusion, type of gastrectomy, and adjuvant chemotherapy across the four groups. Notably, while differences were observed between the groups, the variances between G1 and G2 were not statistically significant, with the exception of G1 exhibiting a shorter duration of illness compared to G2. Compared with G3 and G4, G1 displayed a higher proportion of male patients, individuals with albumin levels below 35 g/L, those undergoing total gastrectomy, and patients who did not receive adjuvant chemotherapy or were limited to 1–3 cycles.

With regard to pathological features, G1 had significantly more upper stomach cancers and histopathological grading 1–2 compared to other groups. However, no significant differences were observed among groups in

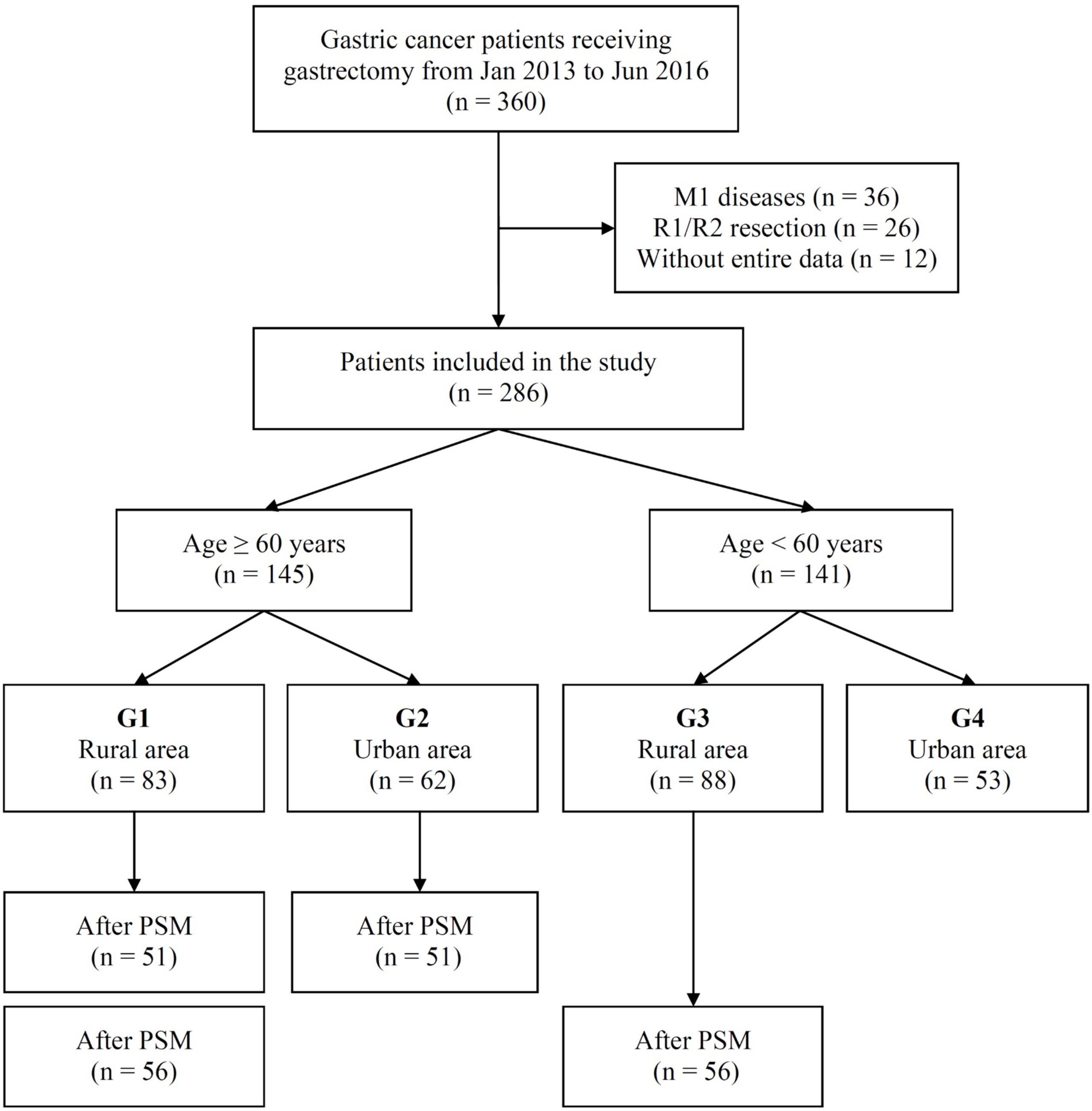

Fig. 1. Patient Selection Flow Diagram. PSM: propensity score matching.

Variables	Total ($n=286$)	Group 1 (G1) rural older ($n=83$)	Group 2 (G2) urban older ($n=62$)	Group 3 (G3) rural younger ($n=88$)	Group 4 (G4) urban younger ($n=53$)	$P_{overall}$	$P_{G1\ vs.\ G2}$*	$P_{G1\ vs.\ G3}$*	$P_{G1\ vs.\ G4}$*
Sex									
Female	76 (26.6)	12 (14.5)	13 (21.0)	28 (31.8)	23 (43.4)	0.001	1.000	0.062	0.001
Male	210 (73.4)	71 (85.5)	49 (79.0)	60 (68.2)	30 (56.6)				
Age (years)	60.0 (28–78)	65.0 (60–76)	67.0 (60–78)	50.0 (28–59)	51.5 (30–59)	< 0.001	1.000	< 0.001	< 0.001
Duration of illness (months)	2.0 (0-120.0)	2.0 (0–36.0)	3.0 (0–48.0)	3.0 (0.2–120.0)	2.0 (0.1–72.0)	0.114	0.029	0.037	0.376
Comorbidity									
No	221 (77.3)	64 (77.1)	42 (67.7)	75 (85.2)	40 (75.5)	0.091	0.208	0.174	0.826
Yes	65 (22.7)	19 (22.9)	20 (32.3)	13 (14.8)	13 (24.5)				
ASA class									
I	160 (55.3)	36 (43.4)	28 (45.2)	66 (75.0)	30 (56.6)	< 0.001	1.000	< 0.001	0.746
II	121 (43.1)	46 (55.4)	30 (48.4)	22 (25.0)	23 (43.4)				
II	5 (1.7)	1 (1.2)	4 (6.5)	0 (0)	0 (0)				
Body mass index									
<18.5 kg/m^2	21 (7.3)	6 (7.2)	5 (8.1)	7 (8.0)	3 (5.7)	0.001	1.000	0.286	0.003
18.5–24 kg/m^2	176 (61.5)	59 (71.1)	44 (71.0)	50 (56.8)	23 (43.4)				
≥24 kg/m^2	89 (31.1)	18 (21.7)	13 (21.0)	31 (35.2)	27 (50.9)				
Hemoglobin									
<90 g/L	44 (15.4)	11 (13.3)	13 (21.0)	11 (12.5)	9 (17.0)	0.488	0.216	0.883	0.549
≥90 g/L	242 (84.6)	72 (86.7)	49 (79.0)	77 (87.5)	44 (83.0)				
Albumin (g/L)									
<35 g/L	29 (10.1)	11 (13.3)	14 (22.6)	3 (3.4)	1 (1.9)	< 0.001	0.397	0.200	0.195
≥35 g/L	257 (89.9)	71 (86.7)	48 (77.4)	85 (96.6)	52 (98.1)				
Perioperative blood transfusion									
No	213 (74.5)	59 (71.1)	39 (62.9)	73 (83.0)	42 (79.2)	0.032	1.000	0.454	1.000
Yes	73 (25.5)	24 (28.9)	23 (37.1)	15 (17.0)	11 (20.8)				
Type of gastrectomy									
Distal	127 (44.4)	23 (27.7)	29 (46.8)	42 (47.7)	33 (62.3)	0.001	0.157	0.037	< 0.001
Total	148 (51.7)	55 (66.3)	30 (48.4)	44 (50.0)	19 (35.8)				
Proximal	11 (3.8)	5 (6.0)	3 (4.8)	2 (2.3)	1 (1.9)				
Adjuvant chemotherapy	4.0 (1–15)	3.0 (1–11)	4.0 (1–8)	4.5 (1–11)	5.0 (1–11)	< 0.001	0.349	0.015	< 0.001
≥4 cycles	143 (50.0)	27 (32.5)	30 (48.4)	48 (54.5)	38 (71.7)	0.001	0.314	0.046	0.001
1–3 cycles	99 (34.6)	38 (45.8)	24 (38.7)	28 (31.8)	9 (17.0)				
0 cycle	28 (9.8)	16 (19.3)	6 (9.7)	6 (6.8)	0 (0)				
Unnecessary	16 (5.6)	2 (2.4)	2 (3.2)	6 (6.8)	6 (11.3)				
Tumor location									
Lower	168 (58.7)	34 (41.0)	39 (62.9)	54 (61.4)	41 (77.4)	< 0.001	0.031	0.009	< 0.001
Middle	38 (13.3)	10 (12.0)	6 (9.7)	14 (15.9)	8 (15.1)				
Upper	80 (28.0)	39 (47.0)	17 (27.4)	20 (22.7)	4 (7.5)				
Tumor size									
<4 cm	91 (31.8)	19 (22.9)	20 (32.3)	25 (28.4)	27 (50.9)	0.006	1.000	1.000	0.004
≥4 cm	195 (68.2)	64 (77.1)	42 (67.7)	63 (71.6)	26 (49.1)				
Macroscopic type									
Type 0/1/2	181 (63.3)	52 (62.7)	40 (64.5)	53 (60.2)	36 (67.9)	0.826	0.817	0.745	0.530
Type 3/4	105 (36.7)	31 (37.3)	22 (35.5)	35 (39.8)	17 (32.1)				
Histopathological grading									
G1-2	142 (49.7)	56 (67.5)	33 (53.2)	34 (38.6)	19 (35.8)	< 0.001	0.541	0.001	0.002
G3-4	144 (50.3)	27 (32.5)	29 (46.8)	54 (61.4)	34 (64.2)				
Lymphatic/Venous invasion									
No	177 (61.9)	48 (57.8)	41 (66.1)	54 (61.4)	34 (64.2)	0.759	0.310	0.638	0.463
Yes	109 (38.1)	35 (42.2)	21 (33.9)	34 (38.6)	19 (35.8)				
Perineural invasion									
No	184 (64.3)	50 (60.2)	43 (69.4)	56 (63.6)	35 (66.0)	0.713	0.258	0.648	0.496
Yes	102 (35.7)	33 (39.8)	19 (30.6)	32 (36.4)	18 (34.0)				
pT category									
T1-2	48 (16.8)	11 (13.3)	9 (14.5)	16 (18.2)	12 (22.6)	0.251	0.451	0.655	0.330
Continued									

Variables	Total (*n* = 286)	Group 1 (G1) rural older (*n* = 83)	Group 2 (G2) urban older (*n* = 62)	Group 3 (G3) rural younger (*n* = 88)	Group 4 (G4) urban younger (*n* = 53)	$P_{overall}$	$P_{G1 vs. G2}$*	$P_{G1 vs. G3}$*	$P_{G1 vs. G4}$*
T3-4a	206 (72.0)	63 (75.9)	42 (67.7)	64 (72.7)	37 (69.8)				
T4b	32 (11.2)	9 (10.8)	11 (17.7)	8 (9.1)	4 (7.5)				
pN category									
N0	76 (26.6)	17 (20.5)	14 (22.6)	29 (33.0)	16 (30.2)	0.436	0.288	0.308	0.293
N1	70 (24.5)	25 (30.1)	14 (22.6)	22 (25.0)	9 (17.0)				
N2	78 (27.3)	20 (24.1)	23 (37.1)	20 (22.7)	15 (28.3)				
N3	62 (21.7)	21 (25.3)	11 (17.7)	17 (19.3)	13 (24.5)				
pTNM stage									
I	32 (11.2)	5 (6.0)	6 (9.7)	12 (13.6)	9 (17.0)	0.454	0.678	0.225	0.122
II	66 (23.1)	19 (22.9)	15 (24.2)	21 (23.9)	11 (20.8)				
III	188 (65.7)	59 (71.1)	41 (66.1)	55 (62.5)	33 (62.3)				

Table 1. Patient characteristics and pathological features according to Age-Residence groups. * P-values were adjusted by Bonferroni correction.

tumor size, macroscopic type, lymphatic/venous invasion, perineural invasion, pT category, pN category, or pTNM stage.

In addition, comparisons of patient characteristics and pathological features between older and younger groups, as well as between rural and urban areas are reported in Supplementary Table 1. Briefly, compared with younger patients, older patients were associated with more males, worse ASA class, lower BMI, hypoproteinemia, more perioperative blood transfusions, more upper stomach cancer and total gastrectomy, while less adequate adjuvant chemotherapy. Compared with urban patients, rural patients were associated with more upper stomach cancer and total gastrectomy but less adequate adjuvant chemotherapy, which might be mainly due to older patients.

Survival analysis in all patients

The 5-year OS rate was 60.7% and median OS was not reached in all patients. The 5-year OS rates were 39.9% for G1, 61.1% for G2, 73.1% for G3, and 71.2% for G4. Median OS was 47 months in G1 but not reached in other groups. OS was significantly worse in G1 than other groups (Log rank: overall $P < 0.001$, G1 vs. G2 $P = 0.014$, G1 vs. G3 $P < 0.001$, G1 vs. G4 $P = 0.002$, Fig. 2A. Cox regression: G1 vs. G2: hazard ratio (HR) = 1.832 [95% confidence interval 1.118–3.003], $P = 0.016$, Fig. 2B; G1 vs. G3: HR = 2.666 [1.613–4.407], $P < 0.001$, Fig. 2C; G1 vs. G4: HR = 2.305 [1.318–4.029], $P = 0.003$, Fig. 2D). Additionally, G1 tended to have worse RFS, which was not statistically significant (Log rank: overall $P = 0.088$, Supplementary Fig. 1); nevertheless, when comparing directly with G3, G1 demonstrated a significantly worse RFS (HR = 1.926 [1.129–3.285], $P = 0.016$, Supplementary Fig. 1C). The proportional hazards assumption was tested using Schoenfeld residuals, and no significant violations were observed.

Univariate Cox regression identified age, albumin, perioperative blood transfusion, type of gastrectomy, adjuvant chemotherapy, tumor location, macroscopic type, lymphatic/venous invasion, perineural invasion, pT category, pN category and pTNM stage as prognostic factors; further, multivariate analysis identified age, type of gastrectomy, adjuvant chemotherapy, perineural invasion, pT category and pN category as independent prognostic factors (Table 2).

Survival analysis in older patients

The 5-year OS rate was 49.2% and median OS was 59 months in all older patients. Univariate Cox regression identified residence areas, albumin, type of gastrectomy, adjuvant chemotherapy, macroscopic type, perineural invasion, pT category, pN category and pTNM stage as prognostic factors. Multivariate analysis identified residence areas, adjuvant chemotherapy, pT category and pN category as independent prognostic factors for older patients (Table 3).

After PSM, 102 older patients were included, with 51 each in rural and urban groups. The SMD for most covariates were below 0.1, indicating good balance between the matched groups and there was no significant difference in clinicopathological features (Table 4). Rural older patients exhibited a notably inferior OS compared to urban older patients (HR = 2.269 [1.274–4.042], $P = 0.005$, Fig. 3A). Meanwhile, rural older patients tended to have worse RFS (HR = 1.919 [0.987–3.731], $P = 0.055$, Supplementary Fig. 2A).

Survival analysis in rural patients

The 5-year OS rate was 57.1% and median OS was not reached in all rural patients. Univariate Cox regression identified age, albumin, type of gastrectomy, macroscopic type, lymphatic/venous invasion, perineural invasion, pT category, pN category and pTNM stage as prognostic factors. Multivariate analysis identified age, perineural invasion, pT category and pN category as independent prognostic factors for rural patients (Table 3).

After PSM, 112 rural patients were included, with 56 each in older and younger groups. The SMD for most covariates were below 0.1, indicating good balance between the matched groups and there was no significant difference in clinicopathological features, except for less patients receiving ≥ 4 cycles of adjuvant chemotherapy

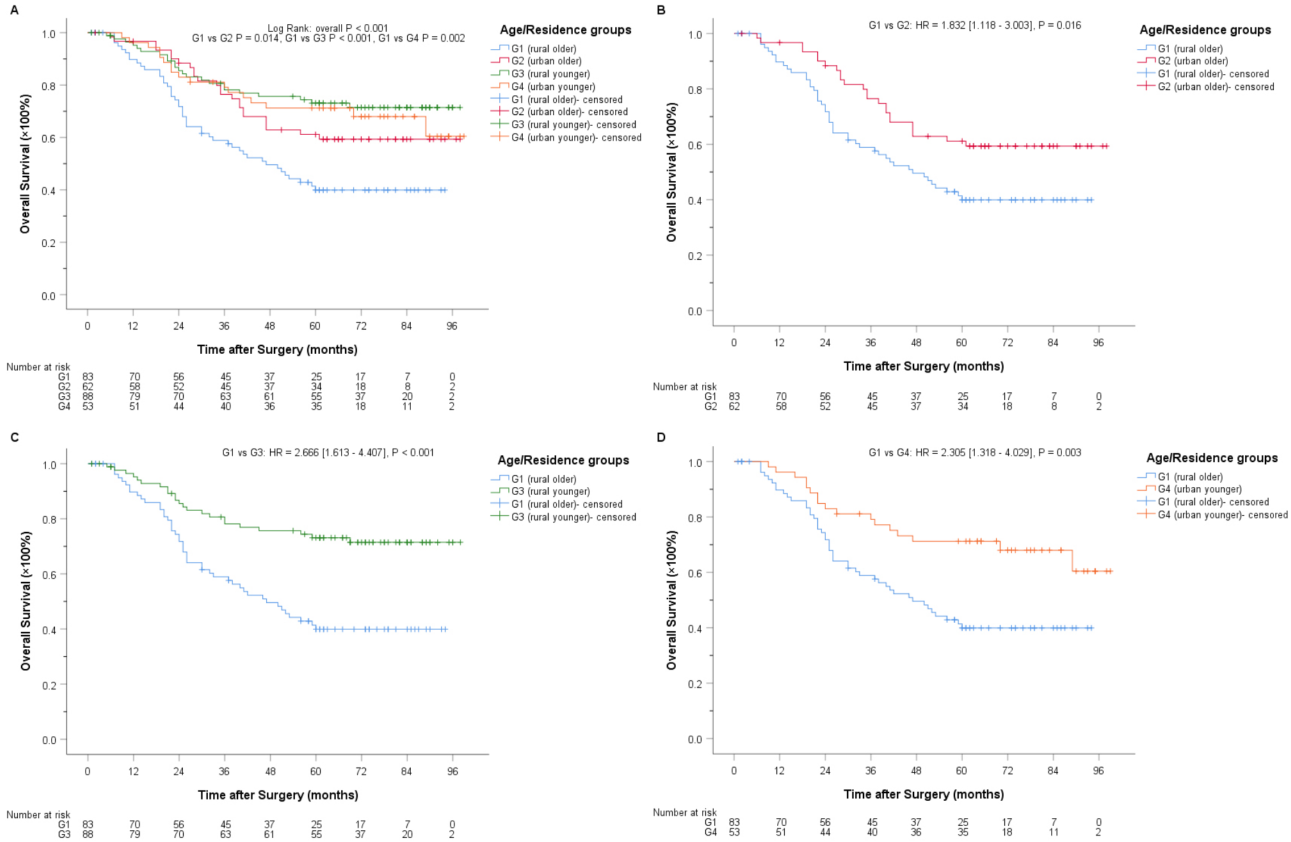

Fig. 2. Overall Survival in All Patients according to Age-Residence Groups. (**A**) Kaplan-Meier analysis of overall survival for four age-residence groups; (**B**) Comparison of overall survival between G1 (rural older) and G2 (urban older); (**C**) Comparison of overall survival between G1 (rural older) and G3 (rural younger); (**D**) Comparison of overall survival between G1 (rural older) and G4 (urban younger).

in older patients (Table 4). Rural older patients exhibited a notably inferior OS compared to rural younger patients (HR = 2.103 [1.116–3.961], P = 0.021, Fig. 3B). Similarly, rural older patients tended to have worse RFS (HR = 1.812 [0.944–3.477], P = 0.074, Supplementary Fig. 2B).

Discussion

The present study found that OS of rural older gastric cancer patients was significantly inferior to that of their urban older and rural younger counterparts, which was confirmed by controlling for confounding factors through PSM analysis. We explored the potential factors contributing to this disparity through comparing the clinicopathological features across different groups and performing Cox regression analysis. The study did not attribute the differences in OS between rural and urban older patients to delayed diagnosis or advanced TNM stage in rural patients. Instead, the analysis revealed that rural older patients were more likely to have upper stomach cancers and undergo total gastrectomy, while less likely to receive adequate adjuvant chemotherapy compared to their urban older or rural younger counterparts. These factors may have contributed to the increased fatality rates observed in rural older patients.

The identification of age as an independent prognostic factor in patients undergoing curative-intent therapy for stomach cancer is consistent with previous studies[16–18]. However, the current study found that there was no significant difference in OS between urban older patients and urban or rural younger patients. Indeed, advancements in surgical techniques, including the use of minimally invasive surgery and lymph node dissection preserving the spleen and pancreas, have made age no longer a limiting factor in radical gastrectomy. Gastrectomy with lymph node dissection did not significantly increase postoperative complications in older patients. However, older patients still had worse OS outcomes after both D1 and D2 lymph node dissection compared to younger patients, and D2 dissection did not provide a significant survival benefit for older patients[19–22]. This indicates that the poor prognosis in older patients cannot be solely attributed to the surgical procedure itself, but rather to other factors that may accompany aging, such as functional status, comorbidities, nutritional status and frailty[23,24]. The older patients in this study exhibited higher ASA scores, a lower proportion of high BMI, and more cases of hypoproteinemia, highlighting the importance of comprehensive assessments of older patients in the perioperative period. These factors can impact the patient's ability to tolerate treatment, recover from surgery, and ultimately affect their overall prognosis. Therefore, it is crucial to consider these

Variables	Univariate analysis HR (95% CI)	*P*	Multivariate analysis HR (95% CI)	*P*
Sex (Male vs. Female)	1.148 (0.739–1.783)	0.539		
Age (≥ 60 vs. < 60 years)	1.977 (1.339–2.917)	0.001	1.547 (1.028–2.328)	0.036
Residence areas (Rural vs. Urban)	1.283 (0.872–1.889)	0.206		
Duration of illness (≥ 2 vs. < 2 months)	0.789 (0.542–1.148)	0.216		
Comorbidity (Yes vs. No)	1.121 (0.730–1.722)	0.602		
ASA class		0.722		
I	1			
II	1.114 (0.761–1.631)	0.578		
III	1.481 (0.464–4.729)	0.507		
Body mass index		0.237		
18.5–24 kg/m^2	1			
<18.5 kg/m^2	1.217 (0.628–2.360)	0.561		
≥24 kg/m^2	0.725 (0.471–1.117)	0.145		
Hemoglobin (< 90 vs. ≥ 90 g/L)	1.291 (0.802–2.078)	0.292		
Albumin (< 35 vs. ≥ 35 g/L)	2.058 (1.239–3.418)	0.005		
Perioperative blood transfusion (Yes vs. No)	1.555 (1.046–2.311)	0.029		
Type of gastrectomy		< 0.001		0.001
Distal	1		1	
Total	3.001 (1.946–4.629)	< 0.001	2.296 (1.464-3.600)	< 0.001
Proximal	2.214 (0.855–5.734)	0.102	2.161 (0.806–5.797)	0.126
Adjuvant chemotherapy		0.018		0.008
≥4 cycles	1		1	
1–3 cycles	1.445 (0.959–2.177)	0.078	1.546 (1.015–2.353)	0.042
0 cycle	2.351 (1.369–4.039)	0.002	2.063 (1.172–3.632)	0.012
Tumor location		0.001		
Lower	1			
Middle	1.475 (0.841–2.587)	0.175		
Upper	2.160 (1.439–3.242)	< 0.001		
Tumor size (≥ 4 vs. < 4 cm)	1.328 (0.868–2.030)	0.191		
Macroscopic type (Type 3/4 vs. Type 0/1/2)	2.272 (1.562–3.305)	< 0.001		
Histopathological grading (G3-4 vs. G1-2)	0.942 (0.648–1.370)	0.755		
Lymphatic/Venous invasion (Yes vs. No)	1.539 (1.058–2.240)	0.024		
Perineural invasion (Yes vs. No)	2.135 (1.468–3.106)	< 0.001	1.768 (1.181–2.645)	0.006
pT category		< 0.001		0.007
T1-2	1		1	
T3-4a	3.271 (1.510–7.084)	0.003	1.374 (0.611–3.090)	0.443
T4b	8.264 (3.541–19.287)	< 0.001	2.868 (1.182–6.958)	0.020
pN category		< 0.001		< 0.001
N0	1		1	
N1	1.694 (0.843–3.406)	0.139	0.909 (0.445–1.855)	0.793
N2	3.017 (1.599–5.693)	0.001	1.610 (0.831–3.120)	0.158
N3	5.134 (2.746–9.599)	< 0.001	2.866 (1.487–5.523)	0.002
pTNM stage		< 0.001		
I	1			
II	4.434 (1.014–19.390)	0.048		
III	10.690 (2.633–43.396)	0.001		

Table 2. Cox regression for overall survival in all patients.

additional conditions and factors when managing older patients with stomach cancer to optimize outcomes and provide appropriate support during the treatment process[24].

Gastric cancer can be categorized into two topographical subsites, the cardia (upper stomach) and noncardia (lower stomach), each with distinct risk factors, carcinogenesis, epidemiologic patterns and prognosis[25]. Upper stomach cancer, typically located in the cardia region, is associated with specific characteristics that may correlate with a worse prognosis compared to lower stomach cancer. Patients with upper stomach cancer often present with a higher prevalence of males, older age, and more advanced pathological stages upon diagnosis[26,27]. These less favorable clinicopathological features can significantly impact treatment options and overall prognosis[26–28].

	Older Patients (*n* = 145)				Rural Patients (*n* = 171)			
Variables	**Univariate analysis**		**Multivariate analysis**		**Univariate analysis**		**Multivariate analysis**	
	HR (95% CI)	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Sex (Male vs. Female)	0.925 (0.496–1.722)	0.805			1.104 (0.614–1.987)	0.740		
Age (≥ 60 vs. < 60 years)	Not Applicable		Not Applicable		2.666 (1.613–4.407)	< 0.001	2.714 (1.623–4.538)	< 0.001
Residence areas (Rural vs. Urban)	1.832 (1.118–3.003)	0.016	2.856 (1.612–5.058)	< 0.001	Not Applicable		Not Applicable	
Duration of illness (≥ 2 vs. < 2 months)	0.738 (0.461–1.181)	0.206			0.784 (0.489–1.258)	0.314		
Comorbidity (Yes vs. No)	1.346 (0.817–2.218)	0.243			1.467 (0.857–2.513)	0.163		
ASA class		0.905				0.120		
I	1				1			
II	0.897 (0.555–1.448)	0.656			1.505 (0.935–2.423)	0.092		
III	0.960 (0.294–3.137)	0.947			4.069 (0.552–30.003)	0.169		
Body mass index		0.584				0.779		
18.5–24 kg/m^2	1				1			
<18.5 kg/m^2	1.214 (0.521–2.831)	0.653			1.098 (0.468–2.573)	0.830		
≥24 kg/m^2	0.765 (0.416–1.408)	0.390			0.840 (0.486–1.452)	0.533		
Hemoglobin (< 90 vs. ≥ 90 g/L)	1.307 (0.728–2.349)	0.370			1.504 (0.807–2.803)	0.199		
Albumin (< 35 vs. ≥ 35 g/L)	2.084 (1.214–3.576)	0.008			2.203 (1.089–4.457)	0.028		
Perioperative blood transfusion (Yes vs. No)	1.332 (0.823–2.156)	0.244			1.618 (0.968–2.703)	0.066		
Type of gastrectomy		0.018				0.003		
Distal	1				1			
Total	2.240 (1.273–3.941)	0.005			2.711 (1.521–4.835)	0.001		
Proximal	2.256 (0.826–6.163)	0.112			2.574 (0.854–7.759)	0.093		
Adjuvant chemotherapy		0.015		0.008		0.106		
≥4 cycles	1		1		1			
1–3 cycles	1.759 (1.014–3.051)	0.044	2.258 (1.278–3.991)	0.005	1.608 (0.950–2.724)	0.077		
0 cycle	2.855 (1.503–5.423)	0.001	2.929 (1.509–5.686)	0.001	2.219 (1.134–4.342)	0.020		
Tumor location		0.109				0.067		
Lower	1				1			
Middle	1.295 (0.592–2.834)	0.518			1.207 (0.571–2.551)	0.621		
Upper	1.708 (1.037–2.814)	0.036			1.812 (1.092–3.008)	0.022		
Tumor size (≥ 4 vs. < 4 cm)	1.534 (0.854–2.756)	0.152			1.201 (0.677–2.128)	0.531		
Macroscopic type (Type 3/4 vs. Type 0/1/2)	2.325 (1.453–3.721)	< 0.001			1.687 (1.051–2.707)	0.030		
Histopathological grading (G3-4 vs. G1-2)	0.916 (0.562–1.494)	0.725			0.959 (0.597–1.541)	0.862		
Lymphatic/Venous invasion (Yes vs. No)	1.590 (0.994–2.544)	0.053			1.607 (1.001–2.579)	0.050		
Perineural invasion (Yes vs. No)	1.842 (1.148–2.954)	0.011			2.672 (1.659–4.304)	< 0.001	1.756 (1.054–2.928)	0.031
pT category		< 0.001		< 0.001		< 0.001		< 0.001
T1-2	1		1		1		1	
T3-4a	1.843 (0.788–4.312)	0.159	1.057 (0.438–2.548)	0.903	3.382 (1.222–9.359)	0.019	1.437 (0.479–4.315)	0.518
T4b	4.938 (1.943–12.545)	0.001	4.173 (1.530–11.380)	0.005	12.301 (4.029–37.561)	< 0.001	6.349 (1.968–20.487)	0.002
pN category		< 0.001		< 0.001		< 0.001		0.001
N0	1		1		1		1	
N1	1.588 (0.603–4.177)	0.349	0.772 (0.281–2.117)	0.615	1.849 (0.738–4.636)	0.190	1.245 (0.481–3.224)	0.652
N2	3.846 (1.586–9.328)	0.003	2.527 (0.981–6.509)	0.055	4.235 (1.807–9.929)	0.001	2.887 (1.171–7.119)	0.021
N3	5.652 (2.303–13.869)	< 0.001	4.052 (1.592–10.317)	0.003	6.970 (3.023–16.072)	< 0.001	4.113 (1.686–10.033)	0.002
pTNM stage		0.002				0.002		
I	1				1			
II	3.345 (0.424–26.401)	0.252			4.892 (0.620-38.615)	0.132		
III	9.271 (1.284–66.924)	0.027			12.617 (1.747–91.104)	0.012		

Table 3. Cox regression for overall survival in older patients and rural patients.

In particular, patients with advanced upper stomach cancers are more likely to undergo total gastrectomy, which can have profound effects on dietary intake, nutritional status, psychological well-being and quality of life, potentially reducing their ability to tolerate postoperative adjuvant chemotherapy[29–35]. It's noteworthy that rural older patients had the highest proportion of upper stomach cancer and total gastrectomy in the present study. This finding suggests that this particular patient population may face unique challenges and considerations when it comes to managing upper stomach cancer[36,37]. The combination of advanced disease stage, total gastrectomy,

Variables	Older Patients (*n* = 102)				Rural Patients (*n* = 112)			
	Rural area (*n* = 51)	Urban area (*n* = 51)	*P*	SMD	Older (*n* = 56)	Younger (*n* = 56)	*P*	SMD
Sex								
Male	44 (86.3)	43 (84.3)	0.780	0.055	44 (78.6)	45 (80.4)	0.815	-0.044
Female	7 (13.7)	8 (15.7)			12 (21.4)	11 (19.6)		
Age (years)	67.0 (60–76)	66.0 (60–76)	0.896	0.031	65.0 (60–76)	50.5 (32–59)	< 0.001	NA
Comorbidity								
No	38 (74.5)	36 (70.6)	0.657	-0.087	46 (82.1)	46 (82.1)	1.000	0.000
Yes	13 (25.5)	15 (29.4)			10 (17.9)	10 (17.9)		
ASA class								
I	26 (51.0)	23 (45.1)	0.548	-0.171	34 (60.7)	40 (71.4)	0.231	0.226
II	24 (47.1)	25 (49.0)			22 (39.3)	16 (28.6)		
III	1 (2.0)	3 (5.9)			0 (0)	0 (0)		
Body mass index								
<18.5 kg/m^2	4 (7.8)	4 (7.8)	0.970	0.049	3 (5.4)	6 (10.7)	0.570	-0.030
18.5–24 kg/m^2	36 (70.6)	37 (72.5)			38 (67.9)	35 (62.5)		
≥24 kg/m^2	11 (21.6)	11 (19.6)			15 (26.8)	15 (26.8)		
Hemoglobin								
<90 g/L	8 (15.7)	11 (21.6)	0.445	-0.150	6 (10.7)	7 (12.5)	0.768	-0.055
≥90 g/L	43 (84.3)	40 (78.4)			50 (89.3)	49 (87.5)		
Albumin (g/L)								
<35 g/L	9 (17.6)	9 (17.6)	1.000	0.000	2 (3.6)	3 (5.4)	0.647	-0.086
≥35 g/L	42 (82.4)	42 (82.4)			48 (96.4)	53 (94.6)		
Perioperative blood transfusion								
No	36 (70.6)	32 (62.7)	0.401	-0.165	43 (76.8)	46 (82.1)	0.483	0.132
Yes	15 (29.4)	19 (37.3)			13 (23.2)	10 (17.9)		
Type of gastrectomy								
Distal	17 (33.3)	22 (43.1)	0.481	0.138	18 (32.1)	20 (35.7)	0.922	0.067
Total	32 (62.7)	26 (51.0)			36 (64.3)	34 (60.7)		
Proximal	2 (3.9)	3 (5.9)			2 (3.6)	2 (3.6)		
Adjuvant chemotherapy								
≥4 cycles	15 (29.4)	23 (45.1)	0.110	0.350	18 (32.1)	32 (57.1)	0.005	0.351
1–3 cycles	23 (45.1)	22 (43.1)			27 (48.2)	18 (32.1)		
0 cycle	12 (23.5)	4 (7.8)			10 (17.9)	2 (3.6)		
Unnecessary	1 (2.0)	2 (3.9)			1 (1.8)	4 (7.1)		
Tumor location								
Lower	26 (51.0)	29 (56.9)	0.833	0.105	27 (48.2)	26 (46.4)	0.876	0.000
Middle	6 (11.8)	5 (9.8)			8 (14.3)	10 (17.9)		
Upper	19 (37.3)	17 (33.3)			21 (37.5)	20 (35.7)		
Tumor size								
<4 cm	15 (29.4)	13 (25.5)	0.657	-0.087	11 (19.6)	13 (23.2)	0.645	0.086
≥4 cm	36 (70.6)	38 (74.5)			45 (80.4)	43 (76.8)		
Macroscopic type								
Type 0/1/2	33 (64.7)	33 (64.7)	1.000	0.000	35 (62.5)	33 (58.9)	0.699	-0.073
Type 3/4	18 (35.3)	18 (35.3)			21 (37.5)	23 (41.1)		
Histopathological grading								
G1-2	33 (64.7)	28 (54.9)	0.313	-0.199	35 (62.5)	28 (50.0)	0.182	-0.252
G3-4	18 (35.3)	23 (45.1)			21 (37.5)	28 (50.0)		
Lymphatic/Venous invasion								
No	29 (56.9)	33 (64.7)	0.417	0.160	30 (53.6)	36 (64.3)	0.249	0.217
Yes	22 (43.1)	18 (35.3)			26 (46.4)	20 (35.7)		
Perineural invasion								
No	34 (66.7)	35 (68.6)	0.832	0.042	33 (58.9)	37 (66.1)	0.435	0.147
Yes	17 (33.3)	16 (31.4)			23 (41.1)	19 (33.9)		
pT category								
T1-2	5 (9.8)	6 (11.8)	0.359	-0.037	7 (12.5)	8 (14.3)	0.752	0.016
Continued								

Variables	Older Patients ($n = 102$)				Rural Patients ($n = 112$)			
	Rural area ($n = 51$)	Urban area ($n = 51$)	*P*	SMD	Older ($n = 56$)	Younger ($n = 56$)	*P*	SMD
T3-4a	40 (78.4)	34 (66.7)			45 (80.4)	42 (75.0)		
T4b	6 (11.8)	11 (21.6)			4 (7.1)	6 (10.7)		
pN category								
N0	11 (21.6)	12 (23.5)	0.375	-0.037	13 (23.2)	21 (37.5)	0.190	0.301
N1	16 (31.40)	10 (19.6)			17 (30.4)	13 (23.2)		
N2	13 (25.5)	20 (39.2)			10 (17.9)	13 (23.2)		
N3	11 (21.6)	9 (17.6)			16 (28.6)	9 (16.1)		
pTNM stage								
I	3 (5.9)	5 (9.8)	0.636	0.187	4 (7.1)	7 (12.5)	0.585	0.187
II	10 (19.6)	12 (23.5)			13 (23.2)	14 (25.0)		
III	38 (74.5)	34 (66.7)			39 (69.6)	35 (62.5)		

Table 4. Clinicopathological features in older and rural patients after propensity score matching. SMD, standardized mean difference; NA, not applicable.

and challenges in receiving and tolerating adjuvant chemotherapy among rural older patients may explain the observed differences in prognosis compared to other groups.

Several phase III randomized controlled trials have demonstrated that postoperative adjuvant chemotherapy could significantly improve OS and RFS in patients with advanced gastric cancer who had undergone D2 gastrectomy[38,39]. Furthermore, the study highlighted the importance of relative dose intensity in determining treatment effectiveness, with higher intensity correlating with better outcomes[39]. Adherence to treatment protocols is highlighted as essential for maximizing therapeutic benefits, as the completion and intensity of chemotherapy significantly impact its efficacy[40,41]. The present study identified adjuvant chemotherapy and relative dose intensity as independent prognostic factors, further emphasizing their influence on patient outcomes. Concerningly, rural older patients had lower rates of receiving adjuvant chemotherapy and completing the recommended number of cycles compared to other groups. This disparity in treatment access and adherence could be a key factor contributing to the poorer prognosis observed in this patient population.

Rurality may have a detrimental impact on the long-term prognosis of cancer patients[42,43]. Living in rural areas is usually associated with an unhealthy diet, poor health awareness, lower socioeconomic status, and limited accessibility to health care. The rural population is known to have limited access to fresh healthy foods, leading to a higher consumption of processed and unhealthy foods. Rural residents in Sichuan, particularly older persons, tend to have dietary preferences for salted meat, Chinese bacon (a special type of processed meat made from cured meat that is then smoked and exposed to the sun), sausage and pickled vegetables, which have been linked to higher gastric cancer mortality rates[44–46]. The older patients in this study were mostly born in the 1940s and 1950s, and had very limited education, especially in rural areas, leading to low health literacy and making it difficult for them to comprehend medical information, adhere to treatment plans, and make informed decisions about their care. In rural areas, older individuals often hold strong beliefs in traditional Chinese medicine and certain health and dietary concepts, which may hinder their willingness to receive adequate modern anti-tumor treatments[47,48]. Rural areas often have fewer healthcare facilities, medical professionals, and specialized cancer treatment centers, which coupled with poverty and limited access to healthcare facilities exacerbates disparities in cancer treatment outcomes[49–52]. Additionally, other potential explanations such as genetic predisposition and environmental factors cannot be ruled out, which may influence the aggressiveness of gastric cancer and the response to treatment. To improve gastric cancer outcomes, it is essential to address these disparities and enhance access to healthcare, education, and resources in rural communities[53].

With the acceleration of urbanization, the phenomenon of left-behind older people in Sichuan is becoming increasingly prominent, potentially accounting for half of the total older population[54]. This situation poses unique challenges and implications for the well-being and quality of life of the older population in rural China[13]. The left-behind older population are particularly vulnerable when faced with a diagnosis of gastric cancer and may encounter physiological, psychological, social and financial difficulties and challenges, which can impact treatment and recovery from gastric cancer[55]. The left-behind older patients may face challenges in treatment compliance due to lack of family support and care. Facing the stress and anxiety of a gastric cancer diagnosis and treatment process, the left-behind older patients may lack necessary psychological and social support, which can impact their emotional well-being and recovery process They may face challenges such as traveling long distances for medical care, financial burdens related to medical expenses, difficulties in obtaining medical information, which can affect their ability to receive proper treatment and manage their condition.

Addressing the needs and challenges of rural older patients in China requires a comprehensive and multi-sectoral approach that involves government agencies, healthcare providers, social service organizations, community groups, and policymakers. Several concrete steps can be taken in clinical practice. Firstly, targeted screening programs should be implemented in rural areas to increase early detection rates. These programs can include regular endoscopic examinations and educational campaigns to raise awareness about the symptoms of gastric cancer. Secondly, financial support initiatives should be developed to help rural patients afford the costs of treatment. This can include subsidies for medical expenses and transportation costs to healthcare facilities.

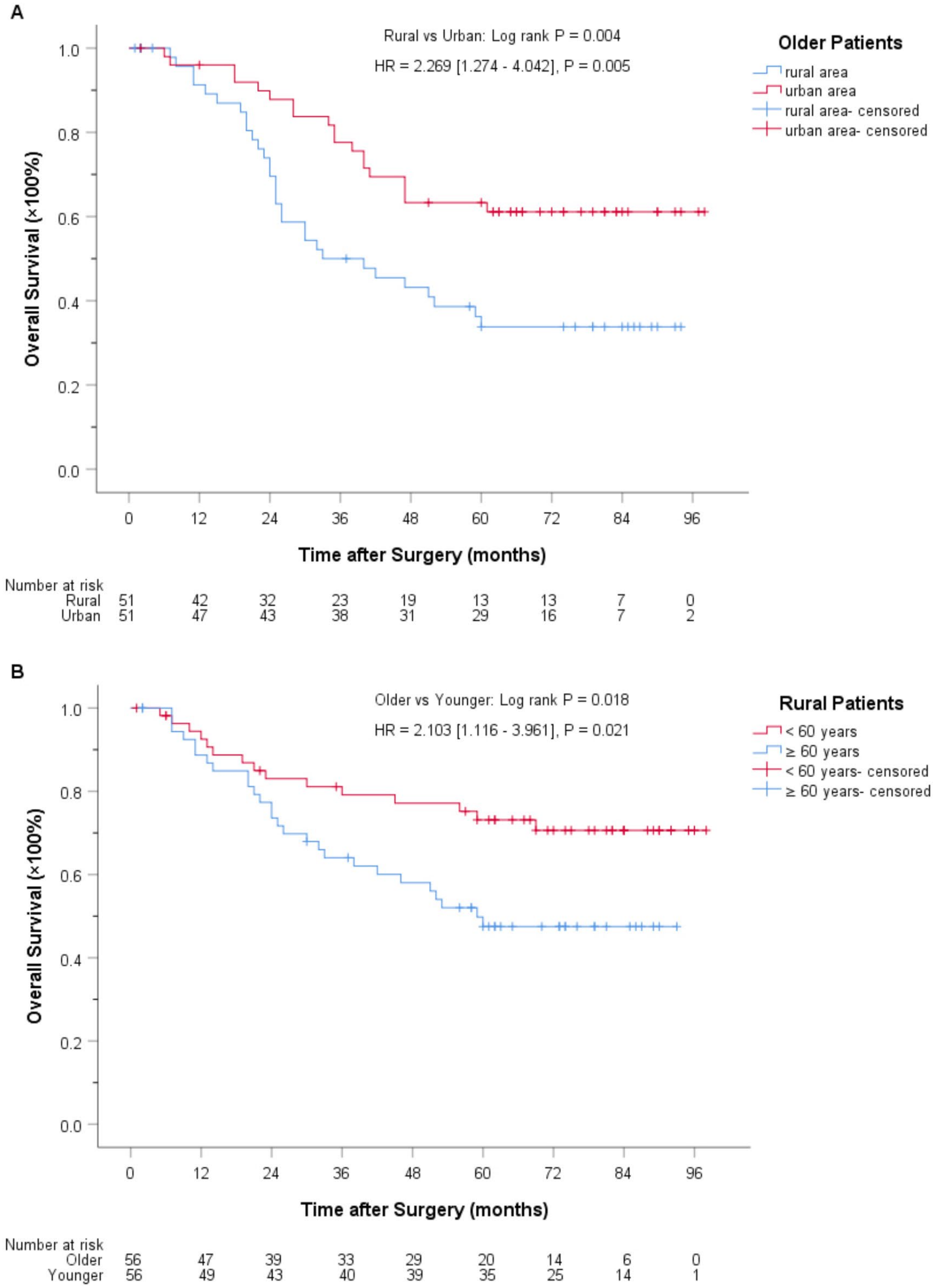

Fig. 3. Comparisons of Overall Survival (**A**) between Rural Older and Urban Older Patients and (**B**) between Rural Older and Rural Younger Patients after Propensity Score Matching.

Thirdly, efforts should be made to improve rural healthcare infrastructure, such as training more healthcare providers and equipping rural hospitals with advanced diagnostic and treatment equipment. These measures can help ensure that rural patients have timely access to high-quality care. Thus, we can help improve their treatment outcomes and quality of life, enabling them to better cope with the challenges of gastric cancer.

The study had several limitations that should be considered when interpreting the results. Firstly, the study was conducted at a single center, which may limit the generalizability of the findings to a broader population.

While these results provided valuable insights into regional disparities, they may not be universally applicable due to the unique socioeconomic and healthcare context of Sichuan. Further studies using external datasets or through multicenter trials are needed to validate these findings in other regions and to explore proactive strategies, such as targeted screening programs and improved access to adjuvant chemotherapy, to address these disparities. Secondly, the retrospective nature of the study may introduce potential bias and confounding variables that were not accounted for in the analysis. The lack of detailed information on socioeconomic status, educational level, and nutritional status scores is a significant limitation. These unmeasured confounders might play a crucial role in influencing treatment access and outcomes in patients with gastric cancer, and their absence in the study limited the understanding of the full spectrum of factors contributing to the observed disparities in outcomes. Thirdly, the small sample size of the study may also impact the statistical power and reliability of the results. Fourthly, there's a potential for misclassification of rural versus urban residence, as some patients may have moved between these areas or may have been inaccurately classified based on their registered permanent address. This misclassification could affect the observed associations between residence and survival outcomes. Additionally, self-selection bias in healthcare-seeking behavior may have influenced the results, as patients who seek medical care may differ systematically from those who do not. Thus, future research with larger sample sizes, prospective study designs, and comprehensive assessments of relevant factors is warranted to further investigate the relationship between age, rurality and outcomes in patients with gastric cancer.

Conclusions

Rural older gastric cancer patients suffered poorer OS after radical gastrectomy. The higher likelihood of upper stomach cancers and total gastrectomy in rural older patients could impact postoperative recovery, nutritional status, and tolerance to treatment. The lower rates of receiving adequate adjuvant chemotherapy might further compromise the effectiveness of treatment and ultimately correlate with poorer outcomes. The study underscores the need to address disparities in gastric cancer care between rural and urban patients, particularly among older individuals. Tailoring treatment approaches to the specific needs and challenges faced by rural older gastric cancer patients, including optimizing surgical strategies, enhancing access to adjuvant chemotherapy, and providing comprehensive support throughout the treatment process, may help improve survival outcomes in this vulnerable population.

Data availability

Research data for this study can be shared upon reasonable request to the corresponding author.

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Author contributions
FQH, XZ and XDC conceived and designed the analysis; FQH, RX and XDC collected the data; DZ and XDC contributed data or analysis tools; FQH and XDC performed the analysis and wrote the paper; All authors read and approved the final manuscript.

Declarations

Competing interests
The authors declare no competing interests.

Ethics approval
This study was approved by the Institutional Review Board of Sichuan Cancer Hospital (SCCSMC-01-2024-110).

Patient consent statement
Written informed consent was waived due to its retrospective design.

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