Original Article

Clinicopathological characteristics and long-term prognosis of duodenal signet ring cell carcinoma: a SEER-based analysis

Jiayi Ding[1], Ye Ye[2], Luojie Liu[2]

[1]Department of Gastroenterology, Changshu Haiyu Central Health Center, Suzhou, China; [2]Department of Gastroenterology, Changshu Hospital Affiliated to Soochow University, Suzhou, China

Contributions: (I) Conception and design: L Liu; (II) Administrative support: None; (III) Provision of study materials or patients: J Ding, Y Ye; (IV) Collection and assembly of data: J Ding, L Liu; (V) Data analysis and interpretation: J Ding, Y Ye; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Luojie Liu, PhD. Department of Gastroenterology, Changshu Hospital Affiliated to Soochow University, No. 1 Shuyuan Street, Suzhou 215500, China. Email: luojieliu@126.com.

Background: Signet ring cell carcinoma (SRCC) of the duodenum represents an exceedingly uncommon and highly aggressive variant of duodenal malignancy. Due to its scarcity, the clinicopathological features and long-term prognostic outcomes of duodenal SRCC remain poorly understood. The present study endeavors to analyze these aspects using data from the Surveillance, Epidemiology, and End Results (SEER) database.

Methods: Patients with duodenal SRCC and adenocarcinoma (AC) diagnosed from 2000 to 2021 were retrieved from the SEER database. Propensity score matching (PSM) approach was used to address confounding factors. The comparison of clinicopathological features was conducted utilizing Chi-squared tests. The evaluation of overall survival (OS) and cancer-specific survival (CSS) was carried out through the application of Kaplan-Meier curves and Cox proportional hazards regression analysis.

Results: A total of 6,132 patients were collected, including 243 with SRCC and 5,889 with AC. SRCC patients were younger, had poorer grade, higher T stage, and more distant (40.7%) and lymph node (39.1%) metastases than AC patients. Age and T stage were risk factors for lymph node metastasis in duodenal SRCC. The 1-, 3-, 5-, and 10-year OS rates for SRCC patients were 42.1%, 22.9%, 17.6%, and 12.1%, respectively, with corresponding CSS rates of 49.4%, 30.1%, 24.4%, and 20.6%. Multivariate Cox regression analysis identified N stage, M stage, surgery, and chemotherapy as significant predictors of OS and CSS. Compared to the no therapy group, the combination of surgery and chemotherapy was optimal for improving OS [hazard ratio (HR): 0.21, 95% confidence interval (CI): 0.14–0.31, P<0.001] and CSS (HR: 0.22, 95% CI: 0.14–0.35, P<0.001). After 1:1 PSM, 243 patient pairs were analyzed; OS (HR: 0.97, 95% CI: 0.80–1.17, P=0.74) and CSS (HR: 0.91, 95% CI: 0.74–1.13, P=0.40) were comparable between SRCC and AC groups.

Conclusions: Despite distinct clinicopathological features, duodenal SRCC and AC share similar long-term prognoses. Surgery plus chemotherapy is optimal for improving outcomes in SRCC.

Keywords: Signet ring cell carcinoma (SRCC); duodenal; clinicopathological characteristics; prognosis; Surveillance, Epidemiology, and End Results (SEER)

Submitted Jul 21, 2025. Accepted for publication Sep 18, 2025. Published online Nov 26, 2025.
doi: 10.21037/tcr-2025-1595
View this article at: https://dx.doi.org/10.21037/tcr-2025-1595

Introduction

Duodenal tumors are rare, comprising only 0.3–0.5% of all gastrointestinal neoplasms and 25–45% of small intestinal tumors (1-3). While most duodenal tumors are adenocarcinomas (ACs), signet ring cell carcinoma (SRCC) is an exceptionally rare subtype, accounting for only about 1% of cases (4,5). Although SRCC occurs most frequently in the stomach, it can also arise in other organs including

the duodenum (6,7).

Previous studies using the Surveillance, Epidemiology, and End Results (SEER) database have explored the clinicopathological features and prognosis of SRCC in sites such as the esophagus, stomach, and pancreas (8-14). With the increasing use of endoscopy, detection of duodenal tumors has improved, bringing attention to rare entities like duodenal SRCC. Several case reports and small series have described its clinical presentation and management (15-17). For instance, Kinslow *et al.* (17) reported that SRCC of the ampulla of Vater carries a poorer prognosis compared to other ampullary cancers.

However, despite these reports, there remains a lack of large-scale, population-based studies specifically focused on the clinicopathological attributes and long-term prognostic trends of duodenal SRCC. Therefore, the objective of this current study is to bridge this knowledge void by leveraging the SEER database to conduct a thorough analysis of duodenal SRCC, aiming to furnish valuable insights that could inform clinical strategies and enhance patient care outcomes. We present this article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1595/rc).

Methods

Patient selection

This study centered on individuals diagnosed with duodenal SRCC and AC from 2000 to 2021, drawing upon data extracted from the SEER database. Patient selection was achieved through the application of ICD-O-3 (International Classification of Diseases for Oncology, Third Edition) codes, with 8490/3 assigned to SRCC cases and 8140/3 to AC cases. Patients without definitive pathological confirmation or lacking comprehensive survival data were systematically excluded from the analysis. A rigorous set of inclusion criteria was applied to the initial patient pool, and the detailed methodological framework is visually represented in the flowchart depicted in *Figure 1*. A range of variables were scrutinized, encompassing patient age, sex, racial background, tumor grade, tumor-node-metastasis (TNM) staging, surgical intervention status, chemotherapy administration, marital status, overall survival (OS), cancer-specific survival (CSS), and follow-up duration. The X-tile software was employed to determine the most suitable age cutoff, as illustrated in *Figure 2*, which facilitated the division of patients into two distinct age cohorts: individuals aged 78 years or below (designated as non-elderly) and those exceeding 78 years (classified as elderly). Racial classification was divided into white, black, or other (incorporating American Indian/Alaska Native and Asian/Pacific Islander populations). Marital status was segmented into married and unmarried groups, with the unmarried category encompassing individuals who were divorced, separated, single, or widowed. The primary objective of this investigation was to assess the clinicopathological features and prognostic outcomes associated with duodenal SRCC. OS and CSS were computed from the date of SRCC diagnosis up to the earliest instance of death, death due to cancer, or the end of the follow-up period. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments.

Statistical analysis

Categorical variables were presented through frequency distributions along with their respective percentages, and Chi-squared tests were utilized to assess disparities among groups. For continuous variables that deviated from normal distribution, the median and interquartile range (IQR) was provided, and comparisons were carried out using the Mann-Whitney *U* test. To bolster the statistical analysis, especially in managing missing data in the SEER dataset, an advanced methodology was employed, which combined multiple imputation (MI) with the random forest technique. To facilitate comparison between the

Highlight box

Key findings

- Based on a Surveillance, Epidemiology, and End Results (SEER) analysis, duodenal signet ring cell carcinoma (SRCC) presents with aggressive features but, after propensity score matching, shows comparable long-term survival to adenocarcinoma (AC), with surgery combined with chemotherapy being the optimal treatment.

What is known and what is new?

- SRCC is a rare, aggressive duodenal tumor subtype, generally associated with a poor prognosis compared to common ACs.
- This large SEER-based study reveals that after balancing confounders, duodenal SRCC and AC have comparable prognoses, and surgery combined with chemotherapy is the optimal treatment.

What is the implication, and what should change now?

- The comparable prognosis suggests that timely diagnosis and aggressive multimodal therapy, not histology alone, should guide management of duodenal SRCC, emphasizing combined surgery and chemotherapy.

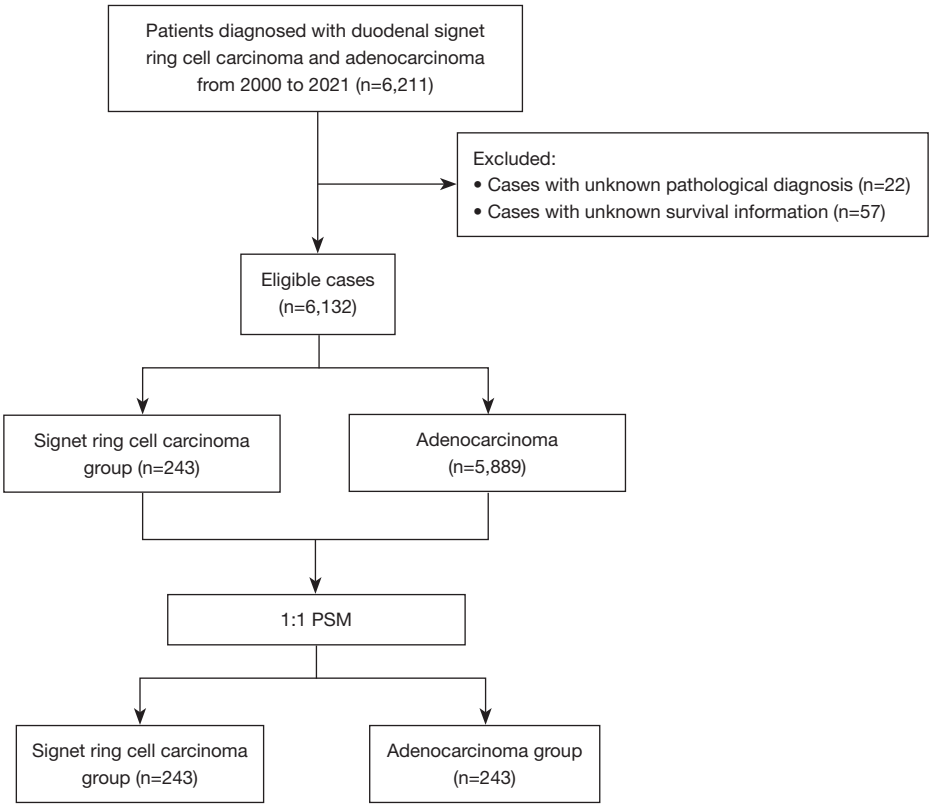

Figure 1 Visual flow diagram illustrating the study design. PSM, propensity score matching.

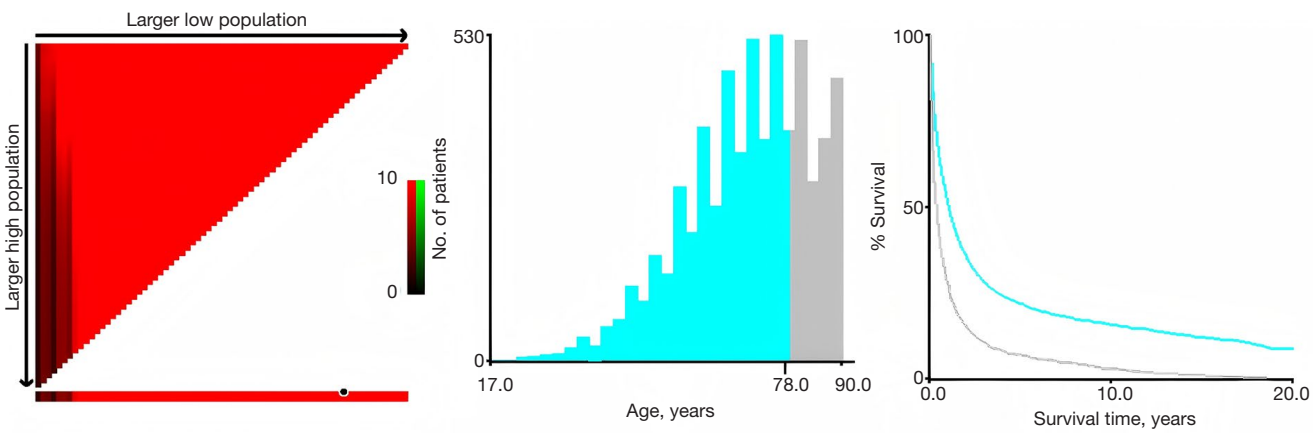

Figure 2 The age distribution at the time of diagnosis among duodenal SRCC and AC patients within the SEER cohort is visually represented using an X-tile plot. Blue represents patients aged 78 or younger, and gray represents patients over 78 years old. AC, adenocarcinoma; SEER, Surveillance, Epidemiology, and End Results; SRCC, signet ring cell carcinoma.

SRCC and AC cohorts, a 1:1 propensity score matching (PSM) approach was implemented, taking into account variables like age, gender, race, tumor grade, TNM stage, surgical intervention status, chemotherapy administration, and marital status, with a caliper set at 0.01. The Kaplan-Meier approach was employed to assess survival outcomes, specifically OS and CSS. Meanwhile, the log-rank test was utilized to evaluate disparities in survival distributions.

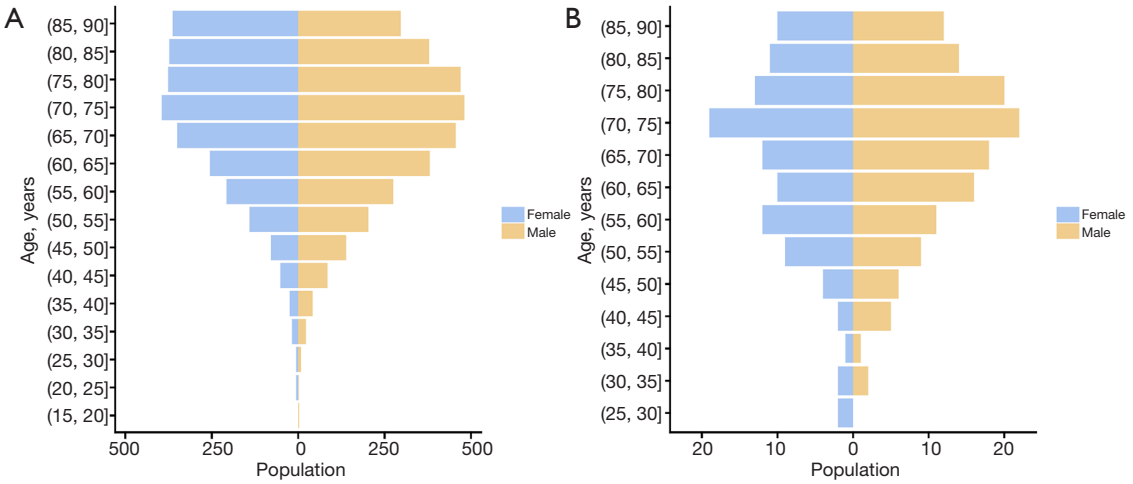

Figure 3 Distribution of patient numbers by age and gender for duodenal SRCC and AC patients in a pyramid chart. (A) SRCC; (B) AC. AC, adenocarcinoma; SRCC, signet ring cell carcinoma.

Both univariate and multivariate Cox proportional hazards models were constructed to compute hazard ratios (HRs) along with their corresponding 95% confidence intervals (CIs). Variables that attained statistical significance (P<0.05) in the univariate analysis were subsequently included in the following multivariate Cox regression model. Additionally, a univariate analysis was carried out to pinpoint potential risk factors associated with lymph node metastases. Variables that demonstrated significance (P<0.05) in this initial evaluation were then subjected to further investigation using a multivariate logistic regression model. All statistical analyses were conducted using R software (version 4.1.0), and statistical significance was set at P<0.05.

Results

Patients characteristics

A total of 6,132 individuals were recruited, comprising 243 with SRCC and 5,889 with AC. Among the duodenal SRCC patients, males outnumbered females (56.0% *vs.* 44.0%). The predominant ethnicity was Caucasian (79.4%), and the majority of tumors were poorly differentiated (91.4%). The largest proportion of patients presented with T stage T4 (39.5%), along with high rates of distant (40.7%) and lymph node (39.1%) metastasis. Surgical intervention was performed on only 36.2% of patients, while 37.4% received chemotherapy. In comparison to duodenal AC, SRCC patients were of younger age, had lower tumor differentiation, advanced T stages, and higher rates of distant and lymph node metastasis. The age-sex pyramid chart shows that the highest number of patients with duodenal SRCC and AC are in the 70–75 years old age group (*Figure 3*). *Table 1* summarizes the clinicopathological characteristics of both duodenal SRCC and AC patients. After 1:1 PSM, no significant differences in baseline characteristics were observed between the SRCC and AC groups (P>0.05). Table S1 offers a comprehensive breakdown of the patients' clinicopathological characteristics prior to MI, emphasizing the presence of missing data: race information was absent in 0.3% of the cases, tumor grade details were lacking in 25.1%, T stage data was incomplete in 13.0%, N stage information was missing in 12.9%, M stage data was unavailable in 12.9%, details on surgical treatment were omitted in 0.5%, and marital status information was not provided in 5.3% of the instances.

Survival analysis of patients with duodenal SRCC and AC

The 1-, 3-, 5-, and 10-year OS rates for duodenal AC patients were 42.1%, 22.9%, 17.6%, and 12.1%, while the corresponding CSS rates were 49.4%, 30.1%, 24.4%, and 20.6%. For duodenal SRCC patients, the OS rates at these same time points were 34.7%, 15.3%, 10.8%, and 7.0% respectively, with CSS rates of 44.0%, 21.4%, 17.7%, and 16.8% (*Table 2*). Prior to PSM, duodenal SRCC patients had significantly worse OS (HR: 1.26, 95% CI: 1.10–1.45, P=0.001) (*Figure 4A*) and CSS (HR: 1.25, 95% CI: 1.07–

Table 1 Comparison of the demographic and clinical characteristics of patients with duodenal AC and SRCC before and after PSM

Variables	Before PSM				After PSM		
	Total (n=6,132)	AC group (n=5,889)	SRCC group (n=243)	P value	AC group (n=243)	SRCC group (n=243)	P value
Age (years)				0.03			0.83
≤78	4,318 (70.4)	4,132 (70.2)	186 (76.5)		188 (77.4)	186 (76.5)	
>78	1,814 (29.6)	1,757 (29.8)	57 (23.5)		55 (22.6)	57 (23.5)	
Sex				0.78			0.93
Male	3,379 (55.1)	3,243 (55.1)	136 (56.0)		135 (55.6)	136 (56.0)	
Female	2,753 (44.9)	2,646 (44.9)	107 (44.0)		108 (44.4)	107 (44.0)	
Race				0.08			0.75
White	4,608 (75.1)	4,415 (75.0)	193 (79.4)		187 (77.0)	193 (79.4)	
Black	976 (15.9)	950 (16.1)	26 (10.7)		27 (11.1)	26 (10.7)	
Others	548 (8.9)	524 (8.9)	24 (9.9)		29 (11.9)	24 (9.9)	
Grade				<0.001			0.86
Well	707 (11.5)	706 (12.0)	1 (0.4)		1 (0.4)	1 (0.4)	
Moderately	2,747 (44.8)	2,739 (46.5)	8 (3.3)		8 (3.3)	8 (3.3)	
Poorly	2,586 (42.2)	2,364 (40.1)	222 (91.4)		226 (93.0)	222 (91.4)	
Undifferentiated	92 (1.5)	80 (1.4)	12 (4.9)		8 (3.3)	12 (4.9)	
T stage				0.02			0.99
T1	1,097 (17.9)	1,054 (17.9)	43 (17.7)		44 (18.1)	43 (17.7)	
T2	298 (4.9)	288 (4.9)	10 (4.1)		9 (3.7)	10 (4.1)	
T3	967 (15.8)	943 (16.0)	24 (9.9)		22 (9.1)	24 (9.9)	
T4	1,914 (31.2)	1,818 (30.9)	96 (39.5)		95 (39.1)	96 (39.5)	
Tx	1,856 (30.3)	1,786 (30.3)	70 (28.8)		73 (30.0)	70 (28.8)	
N stage				0.03			0.76
N0	2,986 (48.7)	2,887 (49.0)	99 (40.7)		91 (37.4)	99 (40.7)	
N+	1,991 (32.5)	1,896 (32.2)	95 (39.1)		100 (41.2)	95 (39.1)	
Nx	1,155 (18.8)	1,106 (18.8)	49 (20.2)		52 (21.4)	49 (20.2)	
M stage				0.03			0.71
M0	3,808 (62.1)	3,672 (62.4)	136 (56.0)		142 (58.4)	136 (56.0)	
M1	2,026 (33.0)	1,927 (32.7)	99 (40.7)		91 (37.4)	99 (40.7)	
Mx	298 (4.9)	290 (4.9)	8 (3.3)		10 (4.1)	8 (3.3)	
Surgery				0.81			0.85
Yes	2,265 (36.9)	2,177 (37.0)	88 (36.2)		90 (37.0)	88 (36.2)	
No	3,867 (63.1)	3,712 (63.0)	155 (63.8)		153 (63.0)	155 (63.8)	

Table 1 (*continued*)

Table 1 (*continued*)

Variables	Before PSM				After PSM		
	Total (n=6,132)	AC group (n=5,889)	SRCC group (n=243)	P value	AC group (n=243)	SRCC group (n=243)	P value
Chemotherapy				0.63			0.93
Yes	2,388 (38.9)	2,297 (39.0)	91 (37.4)		90 (37.0)	91 (37.4)	
No/unknown	3,744 (61.1)	3,592 (61.0)	152 (62.6)		153 (63.0)	152 (62.6)	
Marital status				0.22			0.64
Married	3,475 (56.7)	3,328 (56.5)	147 (60.5)		142 (58.4)	147 (60.5)	
Unmarried	2,657 (43.3)	2,561 (43.5)	96 (39.5)		101 (41.6)	96 (39.5)	
Survival months	7.0 [2.0, 23.0]	7.0 [2.0, 23.0]	4.0 [1.0, 18.0]	0.02	4.0 [1.0, 13.0]	4.0 [1.0, 18.0]	0.43

Data are presented as n (%) or median [IQR]. Others, American Indian, Alaska Native, Asian/Pacific Islander. AC, adenocarcinoma; IQR, interquartile range; M, metastasis; N, node; PSM, propensity score matching; SRCC, signet ring cell carcinoma; T, tumor.

1.46, P=0.005) (*Figure 4B*) compared to duodenal AC patients. Nevertheless, following PSM, the OS (HR: 0.97, 95% CI: 0.80–1.17, P=0.74) (*Figure 4C*) and CSS (HR: 0.91, 95% CI: 0.74–1.13, P=0.40) (*Figure 4D*) were comparable between the SRCC and AC groups.

Subgroup analysis

Following PSM, subgroup analyses indicated that patients diagnosed with duodenal SRCC and those with duodenal AC exhibited similar OS rates across various subgroups, encompassing age, sex, race, tumor grade, N stage, M stage, surgical intervention status, chemotherapy administration, and marital status. The only exception was in the T3 stage group, where patients with AC had better OS than those with SRCC (P=0.02) (*Figure 5*). Furthermore, across all subgroups including age, sex, race, tumor grade, T stage, N stage, M stage, surgical treatment status, chemotherapy receipt, and marital status, the CSS of patients with SRCC was comparable to that of patients with AC (P>0.05) (*Figure 6*). Figure S1 presents the OS of patients with duodenal SRCC and duodenal AC across different subgroups before PSM, and Figure S2 presents the CSS of these patients before PSM.

Univariate and multivariate Cox regressions

Univariate Cox regression analysis identified age, T stage, N stage, M stage, surgical treatment status, and chemotherapy as significant risk factors influencing the OS of patients with duodenal SRCC. Upon multivariate Cox regression analysis, N stage, M stage, surgical treatment status, and chemotherapy emerged as independent predictors of OS in these patients (*Table 3*). Likewise, the univariate analysis also highlighted age, T stage, N stage, M stage, surgical treatment status, and chemotherapy as risk factors affecting CSS in SRCC patients, with the multivariate analysis confirming N stage, M stage, surgical treatment status, and chemotherapy as independent risk factors for CSS (*Table 4*).

Survival analysis of different treatment methods for duodenal SRCC patients

Treatment modality is a crucial factor influencing the prognosis of duodenal SRCC patients. We further analyzed the impact of different treatment approaches on improving patient outcomes. We found that compared to the no therapy group, the surgery group significantly improved OS (HR: 0.37, 95% CI: 0.25–0.56, P<0.001), and the chemotherapy group also enhanced OS (HR: 0.56, 95% CI: 0.39–0.81, P=0.002). Moreover, the combination of surgery and chemotherapy was the optimal approach for improving OS (HR: 0.21, 95% CI: 0.14–0.31, P<0.001) (*Figure 7A*). Additionally, compared to the no therapy group, the surgery group also improved CSS (HR: 0.45, 95% CI: 0.29–0.69, P<0.001), and the chemotherapy group enhanced CSS as well (HR: 0.57, 95% CI: 0.38–0.87, P=0.009). The combination of surgery and chemotherapy was similarly the best approach for improving CSS (HR: 0.22, 95% CI: 0.14–0.35, P<0.001) (*Figure 7B*).

Table 2 Survival analysis of duodenal AC and SRCC

Survival analysis	Survival (%)	95% CI	
		Lower	Upper
Overall survival rate of AC group			
1-year	42.1	40.9	43.4
3-year	22.9	21.8	24.0
5-year	17.6	16.5	18.7
10-year	12.1	11.1	13.2
Cancer specific survival rate of AC group			
1-year	49.4	48.0	50.8
3-year	30.1	28.8	31.5
5-year	24.4	23.1	25.8
10-year	20.6	19.3	22.1
Overall survival rate of SRCC group			
1-year	34.7	29.1	41.3
3-year	15.3	11.3	20.8
5-year	10.8	7.4	15.9
10-year	7.0	4.0	12.1
Cancer specific survival rate of SRCC group			
1-year	44.0	36.7	50.2
3-year	21.4	16.2	28.3
5-year	17.7	12.8	24.5
10-year	16.8	11.9	23.6

AC, adenocarcinoma; CI, confidence interval; SRCC, signet ring cell carcinoma.

Univariate and multivariate analyses of lymph node metastasis

Univariate analysis conducted on patients with duodenal SRCC revealed that age, T stage, and marital status are significant risk factors that are associated with the development of lymph node metastasis. Through subsequent multivariate analysis, it became evident that age and T stage emerged as significant independent risk factors, substantially impacting the likelihood of lymph node metastasis in individuals diagnosed with duodenal SRCC, as detailed in *Table 5*.

Discussion

In this study, our focus was directed towards patients who received a diagnosis of duodenal SRCC and AC during the period spanning from 2000 to 2021, with the SEER database serving as our primary source of data. To mitigate the impact of potential confounding variables, we applied a PSM method. Our primary results indicated that out of the 6,132 patients included in the study (243 with SRCC and 5,889 with AC), SRCC patients were younger, had a lower grade, a higher T stage, and experienced more distant (40.7%) and lymph node (39.1%) metastases than AC patients. Additionally, age and T stage were identified as risk factors for lymph node metastasis in duodenal SRCC. The OS rates for SRCC patients at 1, 3, 5, and 10 years were 42.1%, 22.9%, 17.6%, and 12.1%, respectively, with corresponding CSS rates of 49.4%, 30.1%, 24.4%, and 20.6%. Multivariate Cox regression analysis revealed that N stage, M stage, surgery, and chemotherapy were

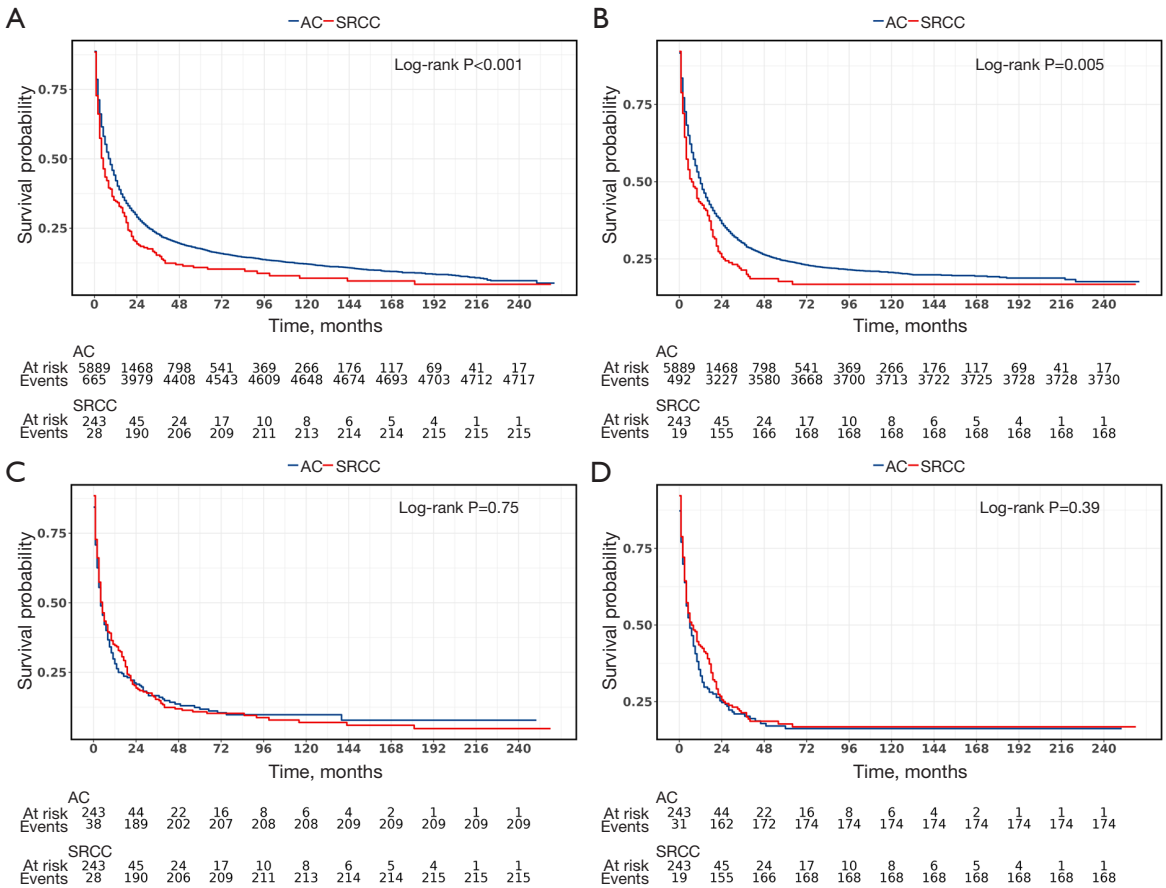

Figure 4 OS and CSS were compared between SRCC group and AC group before and after PSM. (A) OS before PSM; (B) CSS before PSM; (C) OS after PSM; (D) CSS after PSM. AC, adenocarcinoma; CSS, cancer-specific survival; OS, overall survival; PSM, propensity score matching; SRCC, signet ring cell carcinoma.

significant predictors of both OS and CSS. Remarkably, the combination of surgery and chemotherapy proved to be the most effective treatment for enhancing OS and CSS in SRCC patients. Following 1:1 PSM, the OS and CSS were similar between the SRCC and AC groups. Reiterating the objective of our research, we aimed to conduct a thorough investigation into the clinicopathological features and long-term prognostic outcomes of duodenal SRCC by utilizing data from the SEER database. Considering the extreme rarity of duodenal SRCC and the scarce knowledge regarding its clinical and pathological attributes and prognosis, our study plays a crucial role in bridging this knowledge gap.

In previously reported cases, two patients diagnosed with duodenal SRCC were both over 80 years old (15,18). Okamoto *et al.* (16) presented a case of non-ampullary duodenal SRCC in a 61-year-old patient and reviewed the clinicopathological features of 23 duodenal SRCC patients from earlier literature, revealing a median age of 62 years. In contrast, our study found that 50 (20.6%) patients with duodenal SRCC were over 80 years old, with the largest proportion of patients falling within the 70–75 years age group and a median age of 70 years, which is higher than the 62 years reported previously. This discrepancy may stem from differences in sample size and study populations. Nevertheless, our findings confirm that duodenal SRCC predominantly affects individuals over 60 years old, with a lower incidence in younger patients. Consequently, despite the relatively rare occurrence of duodenal tumors, it is crucial to examine the duodenal region during upper gastrointestinal endoscopy in elderly patients and conduct histopathological examinations when necessary.

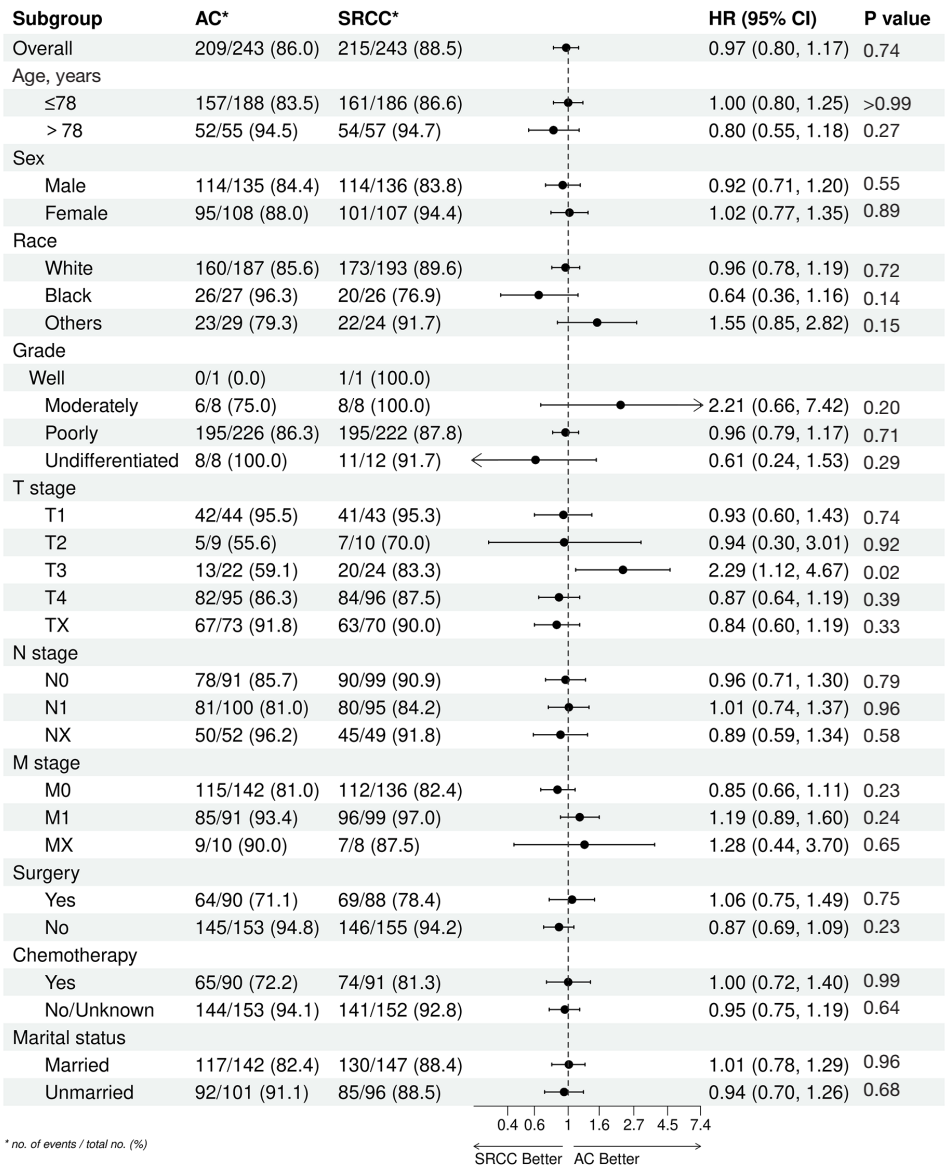

Figure 5 Subgroup analysis of OS between SRCC group and AC group after PSM. AC, adenocarcinoma; CI, confidence interval; HR, hazard ratio; M, metastasis; N, node; OS, overall survival; PSM, propensity score matching; SRCC, signet ring cell carcinoma; T, tumor.

Moreover, our study revealed that 91.4% of duodenal SRCC patients had poorly differentiated tumors, with nearly half (49.4%) classified as T3/T4 stages. Jiang *et al.* (19) analyzed the clinical characteristics of gastric SRCC patients using data from the National Cancer Center and SEER database and reported that the majority of gastric SRCC patients had poorly differentiated tumors (81.5%), with 60.4% at T3 and T4 stages. Similarly, Fung *et al.* (20) examined the clinical data of 53 gastric SRCC patients from their institution and found that 78.9% had poorly differentiated tumors, with 76.7% at T3/T4 stages. These findings indicate that SRCC, whether located in the stomach or duodenum, exhibits poor differentiation and advanced T stages, suggesting an aggressive nature. Additionally, we observed a high risk of distant (40.7%) and lymph node (39.1%) metastases in duodenal SRCC. Age and T stage emerged as risk factors for lymph node metastasis in duodenal SRCC, with a higher T stage

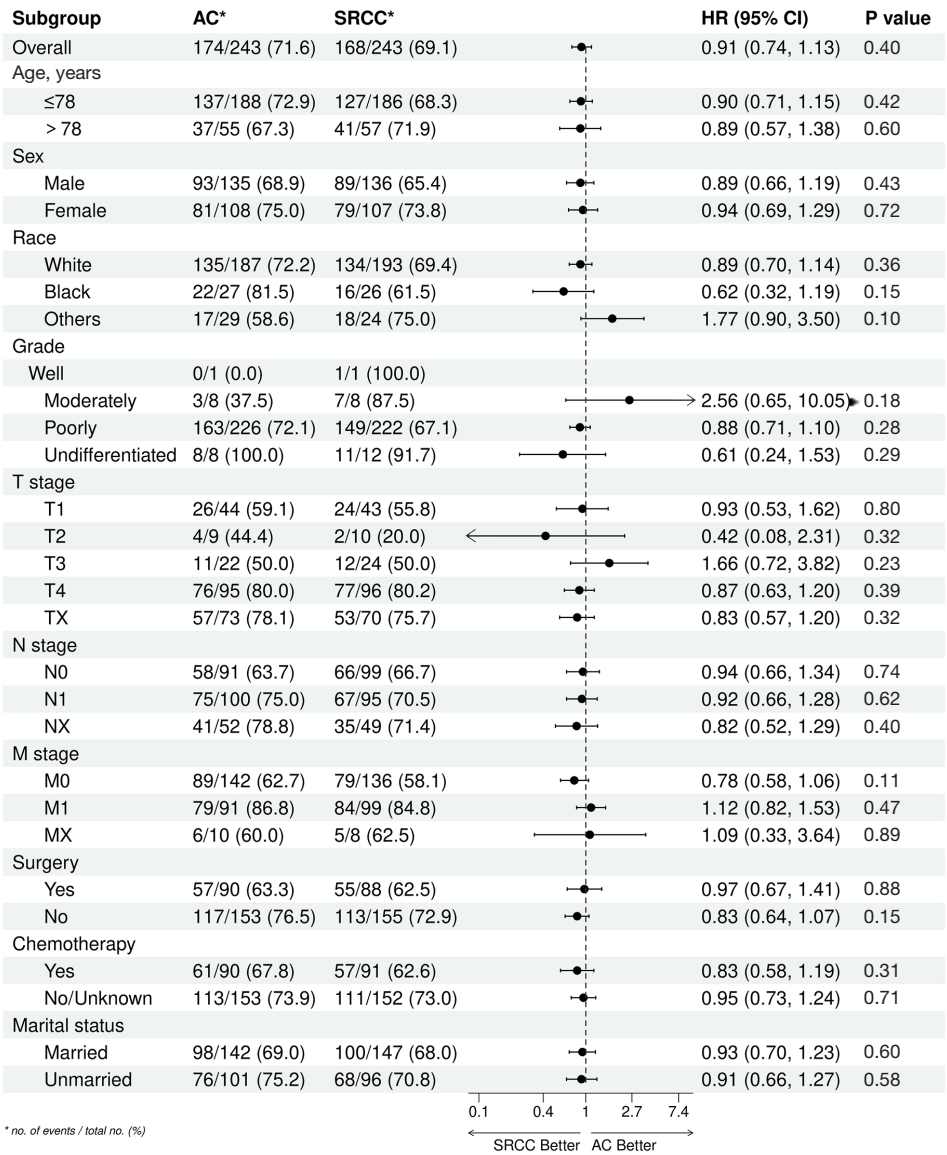

Figure 6 Subgroup analysis of CSS between SRCC group and AC group after PSM. AC, adenocarcinoma; CI, confidence interval; CSS, cancer-specific survival; HR, hazard ratio; M, metastasis; N, node; PSM, propensity score matching; SRCC, signet ring cell carcinoma; T, tumor.

Table 3 Univariate and multivariate cox regression for analyzing the overall survival for patients with duodenal SRCC

Variables	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Age (years)						
≤78	1	Reference		1	Reference	
>78	1.63	1.20, 2.23	0.002	1.29	0.92, 1.81	0.14

Table 3 (*continued*)

Table 3 (*continued*)

Variables	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Sex						
Male	1	Reference		–	–	–
Female	1.24	0.95, 1.62	0.12	–	–	–
Race						
White	1	Reference		–	–	–
Black	0.99	0.62, 1.58	0.97	–	–	–
Others	1.11	0.71, 1.74	0.64	–	–	–
Grade						
Well	1	Reference		–	–	–
Moderately	1.00	0.12, 8.02	>0.99	–	–	–
Poorly	0.98	0.14, 6.98	0.98	–	–	–
Undifferentiated	0.96	0.12, 7.42	0.97	–	–	–
T stage						
T1	1	Reference		1	Reference	
T2	0.23	0.10, 0.51	<0.001	0.51	0.21, 1.23	0.14
T3	0.52	0.31, 0.90	0.02	0.75	0.41, 1.37	0.35
T4	0.63	0.43, 0.92	0.02	0.93	0.59, 1.47	0.75
Tx	1.21	0.81, 1.80	0.35	1.06	0.67, 1.69	0.809
N stage						
N0	1	Reference		1	Reference	
N+	0.72	0.53, 0.97	0.03	1.57	1.06, 2.31	0.02
Nx	1.74	1.21, 2.49	0.003	1.47	0.94, 2.29	0.09
M stage						
M0	1	Reference		1	Reference	
M1	2.94	2.19, 3.94	<0.001	2.96	2.09, 4.18	<0.001
Mx	2.82	1.30, 6.11	0.008	1.93	0.84, 4.45	0.12
Surgery						
Yes	1	Reference		1	Reference	
No	3.06	2.26, 4.14	<0.001	1.85	1.22, 2.82	0.004
Chemotherapy						
Yes	1	Reference		1	Reference	
No/unknown	2.19	1.65, 2.92	<0.001	2.45	1.76, 3.41	<0.001
Marital status						
Married	1	Reference		–	–	–
Unmarried	1.30	0.99, 1.71	0.06	–	–	–

Others: American Indian, Alaska Native, Asian/Pacific Islander. CI, confidence interval; HR, hazard ratios; M, metastasis; N, node; SRCC, signet ring cell carcinoma; T, tumor.

Table 4 Univariate and multivariate cox regression for analyzing the cancer-specific survival for patients with duodenal SRCC

Variables	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Age (years)						
≤78	1	Reference		1	Reference	
>78	1.57	1.10, 2.25	0.01	1.39	0.94, 2.05	0.10
Sex						
Male	1	Reference		–	–	–
Female	1.23	0.91, 1.67	0.18	–	–	–
Race						
White	1	Reference		–	–	–
Black	0.99	0.59, 1.66	0.97	–	–	–
Others	1.13	0.69, 1.85	0.63	–	–	–
Grade						
Well	1	Reference		–	–	–
Moderately	0.84	0.10, 6.87	0.87	–	–	–
Poorly	0.76	0.11, 5.43	0.78	–	–	–
Undifferentiated	1.00	0.13, 7.73	>0.99	–	–	–
T stage						
T1	1	Reference		1	Reference	
T2	0.13	0.03, 0.55	0.006	0.27	0.06, 1.21	0.09
T3	0.56	0.28, 1.12	0.10	0.70	0.33, 1.48	0.35
T4	1.02	0.64, 1.61	0.95	1.35	0.78, 2.32	0.28
Tx	1.71	1.06, 2.78	0.03	1.54	0.89, 2.66	0.12
N stage						
N0	1	Reference		1	Reference	
N+	0.83	0.59, 1.17	0.29	1.64	1.07, 2.52	0.02
Nx	1.83	1.21, 2.78	0.004	1.34	0.82, 2.19	0.24
M stage						
M0	1	Reference		1	Reference	
M1	3.61	2.60, 5.01	<0.001	3.88	2.62, 5.74	<0.001
Mx	2.70	1.09, 6.73	0.03	2.05	0.77, 5.48	0.15
Surgery						
Yes	1	Reference		1	Reference	
No	2.72	1.94, 3.80	<0.001	1.56	1.09, 2.47	0.02
Chemotherapy						
Yes	1	Reference		1	Reference	
No/unknown	2.21	1.60, 3.05	<0.001	2.81	1.95, 4.06	<0.001

Table 4 (*continued*)

Table 4 (*continued*)

Variables	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Marital status						
Married	1	Reference		–	–	–
Unmarried	1.35	0.99, 1.84	0.06	–	–	–

Others: American Indian, Alaska Native, Asian/Pacific Islander. CI, confidence interval; HR, hazard ratios; M, metastasis; N, node; SRCC, signet ring cell carcinoma; T, tumor.

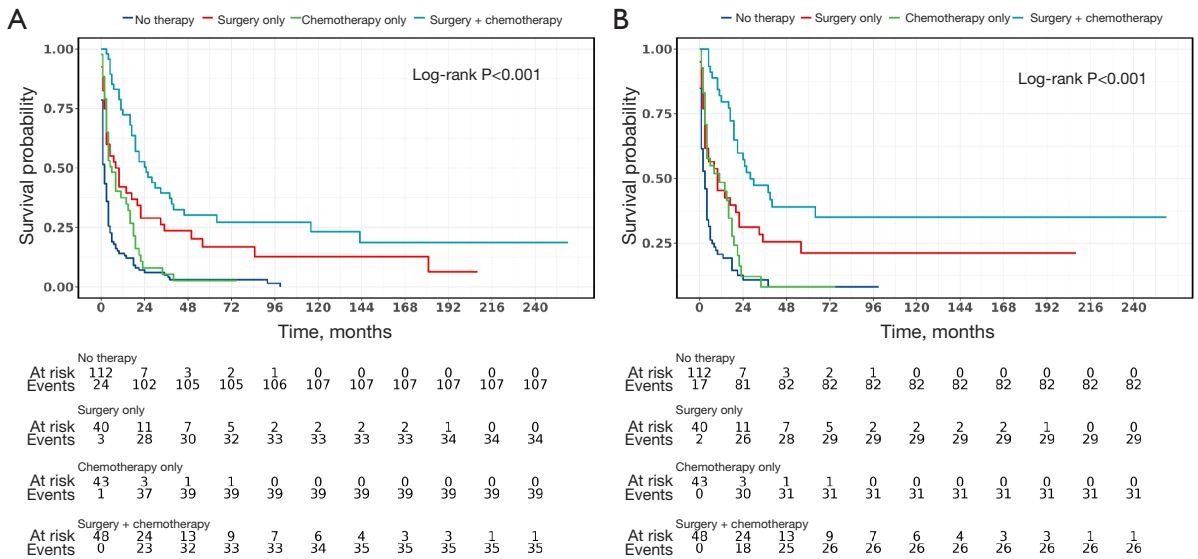

Figure 7 Survival analysis of different treatment methods for duodenal SRCC patients. (A) OS. (B) CSS. CSS, cancer-specific survival; OS, overall survival; SRCC, signet ring cell carcinoma.

associated with an increased risk of metastasis and older age linked to a decreased risk. This phenomenon could potentially be ascribed to the diminished cellular vigor and decreased invasive capacity observed in elderly individuals, which may consequently decelerate the proliferation and spread of cancer cells. Furthermore, elderly patients may prioritize their health and seek medical intervention earlier, contributing to a lower risk of lymph node metastasis. Therefore, younger patients with higher T stages should be prioritized for early screening, diagnosis, and prompt aggressive treatment to mitigate the risk of lymph node metastasis. Conversely, while elderly patients with lower T stages have a relatively lower risk of lymph node metastasis, close monitoring of disease progression and timely intervention remain essential.

Our study identified N stage, M stage, surgery, and chemotherapy as significant risk factors influencing OS and CSS in duodenal SRCC patients. Patients with lymph node or distant metastases exhibited poorer prognoses, whereas those undergoing surgery and chemotherapy demonstrated better outcomes. Yu *et al.* (21) reported that T stage, N stage, M stage, and surgical approach are pivotal factors affecting the prognosis of gastric SRCC, with surgery being the most critical determinant. Similarly, Chu *et al.* (22) found that surgery improves the prognosis of gastrointestinal SRCC patients, regardless of the presence of metastases. Furthermore, we investigated the impact of combined surgery and chemotherapy on the prognosis of duodenal SRCC patients. Our findings revealed that the combination of surgery and chemotherapy was the most

Table 5 Univariate and multivariate analysis of lymph node metastasis in patients with duodenal SRCC

Variables	Univariate			Multivariate		
	OR	95% CI	P value	OR	95% CI	P value
Age (years)						
≤78	1	Reference		1	Reference	
>78	0.11	0.04, 0.28	<0.001	0.17	0.06, 0.47	<0.001
Sex						
Male	1	Reference		–	–	–
Female	0.74	0.42, 1.31	0.30	–	–	–
Race						
White	1	Reference		–	–	–
Black	0.43	0.16, 1.20	0.11	–	–	–
Others	0.77	0.30, 1.95	0.58	–	–	–
Grade						
Well/moderately	1	Reference		–	–	–
Poorly/undifferentiated	1.29	0.28, 5.93	0.74	–	–	–
T stage						
T1	1	Reference		1	Reference	
T2	5.14	0.86, 30.91	0.07	4.29	0.66, 28.01	0.13
T3	21.00	4.86, 90.74	<0.001	15.16	3.34, 68.77	<0.001
T4	31.68	8.95, 112.19	<0.001	24.32	6.58, 89.83	<0.001
Tx	4.70	1.15, 19.19	0.03	3.66	0.86, 15.62	0.08
M stage						
M0	1	Reference		–	–	–
M1	0.75	0.42, 1.35	0.34	–	–	–
Marital status						
Married	1	Reference		1	Reference	
Unmarried	0.48	0.26, 0.86	0.02	0.52	0.25, 1.08	0.08

CI, confidence interval; M, metastasis; N, node; OR, odds ratios; SRCC, signet ring cell carcinoma; T, tumor.

effective treatment modality for improving prognosis, followed by surgery alone and then chemotherapy alone. Ji *et al.* (23) analyzed the effects of surgery and chemotherapy on the prognosis of patients with metastatic gastric SRCC and reported that chemotherapy is the first-line treatment for metastatic SRCC patients, and for those with liver metastases, the combination of surgery and chemotherapy yields optimal outcomes. We posit that the combination of surgery and chemotherapy is optimal for enhancing the prognosis of SRCC patients, likely due to the synergistic effects of surgery in excising the tumor and chemotherapy in eradicating residual lesions, potential metastatic cells, and reducing the risk of drug resistance and recurrence. In contrast, surgery or chemotherapy alone, while beneficial, has limitations, such as incomplete eradication or restricted efficacy. Thus, individualized treatment plans are vital for improving patient prognoses.

Previous studies have reported that SRCC in the colon

and stomach is associated with a worse prognosis compared to AC (21,24,25). Similarly, our unadjusted analysis showed that duodenal SRCC had poorer OS and CSS than duodenal AC, likely due to its aggressive clinicopathological features, including poor differentiation, advanced T stage, and high rates of lymph node and distant metastasis. However, after PSM balanced baseline characteristics such as age, stage, and treatment, the prognosis between SRCC and AC became comparable. This suggests that the apparent worse prognosis of SRCC may be attributable to its more advanced presentation at diagnosis rather than an inherently more aggressive biology. Clinically, this implies that with early detection and standardized treatment, patients with duodenal SRCC can achieve outcomes similar to those with AC. Therefore, efforts should focus on timely diagnosis and aggressive multimodal therapy, rather than assuming a uniformly poor prognosis based on histology alone.

This SEER-based study on duodenal SRCC has several limitations. First, the retrospective design may introduce biases, as data completeness and accuracy rely on the reporting institutions. Second, despite using PSM, unmeasured confounding factors could still affect the comparability between SRCC and AC groups. Third, the relatively small sample size of SRCC patients (n=243) may limit the statistical power and generalizability of the findings. Fourth, the SEER database lacks detailed information regarding specific treatment regimens, such as chemotherapy protocols, radiotherapy details, and surgical techniques. This prevents us from analyzing the impact of particular therapeutic strategies on patient outcomes. Finally, the absence of centralized pathology review means that diagnostic consistency across different institutions could not be verified, potentially introducing variability in the histopathological classification of SRCC and AC. Despite these limitations, there are notable strengths in this study. It provides valuable insights into the clinicopathological characteristics and long-term prognosis of a rare tumor, SRCC, using a large population-based database. The use of PSM enhances the comparability between SRCC and AC groups, and the identification of significant predictors of survival highlights the importance of surgery and chemotherapy in improving outcomes.

Conclusions

In conclusion, our SEER-based analysis has provided valuable insights into the distinct clinicopathological features of duodenal SRCC compared to AC. Despite these differences, both tumor types share similar long-term prognoses after accounting for confounding factors. Our study underscores the importance of surgery combined with chemotherapy as the optimal treatment strategy for improving survival outcomes in SRCC patients. These findings have significant implications for clinical decision-making and pave the way for future research in this rare malignancy.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1595/rc

Peer Review File: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1595/prf

Funding: This study was supported by the Changshu Science and Technology Program (No. CY202339); the Suzhou Youth Science and Technology Project for the Advancement of Science, Education, and Health (No. KJXW2023067); and the Suzhou 23rd Batch of Science and Technology Development Plan (Clinical Trial Institution Capability Enhancement) Project (No. SLT 2023006).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1595/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments.

References

1. Alwmark A, Andersson A, Lasson A. Primary carcinoma of the duodenum. Ann Surg 1980;191:13-8.
2. Vlachou E, Koffas A, Toumpanakis C, et al. Updates in the diagnosis and management of small-bowel tumors. Best Pract Res Clin Gastroenterol 2023;64-65:101860.
3. Kuntz S, Krieghoff-Henning E, Kather JN, et al. Gastrointestinal cancer classification and prognostication from histology using deep learning: Systematic review. Eur J Cancer 2021;155:200-15.
4. Buchbjerg T, Fristrup C, Mortensen MB. The incidence and prognosis of true duodenal carcinomas. Surg Oncol 2015;24:110-6.
5. Legué LM, Bernards N, Gerritse SL, et al. Trends in incidence, treatment and survival of small bowel adenocarcinomas between 1999 and 2013: a population-based study in The Netherlands. Acta Oncol 2016;55:1183-9.
6. Pernot S, Voron T, Perkins G, et al. Signet-ring cell carcinoma of the stomach: Impact on prognosis and specific therapeutic challenge. World J Gastroenterol 2015;21:11428-38.
7. Wu SG, Chen XT, Zhang WW, et al. Survival in signet ring cell carcinoma varies based on primary tumor location: a Surveillance, Epidemiology, and End Results database analysis. Expert Rev Gastroenterol Hepatol 2018;12:209-14.
8. Chen C, Wang Z, Qin Y. Prognosis prediction in esophageal signet-ring-cell carcinoma: a competing risk analysis. BMC Gastroenterol 2023;23:178.
9. Xie R, Lu G, Li L. Clinical features and prognostic factors of esophageal signet ring cell carcinoma: construction and validation of a model based on the SEER database. Transl Cancer Res 2022;11:3674-85.
10. Nie D, Zheng H, An G, et al. Development and validation of a novel nomogram for postoperative overall survival of patients with primary gastric signet-ring cell carcinoma: a population study based on SEER database. J Cancer Res Clin Oncol 2023;149:8593-603.
11. Nie D, Yang J, Zheng H, et al. Survival analysis and individualized prediction of survival benefit for pancreatic signet ring cell carcinoma: a population study based on the SEER database. BMC Gastroenterol 2023;23:62.
12. Nie D, Lan Q, Huang Y, et al. Epidemiology and prognostic analysis of patients with pancreatic signet ring cell carcinoma: a population-based study. BMC Gastroenterol 2022;22:458.
13. Ma J, Meng Y, Zhou X, et al. The Prognostic Significance and Gene Expression Characteristics of Gastric Signet-Ring Cell Carcinoma: A Study Based on the SEER and TCGA Databases. Front Surg 2022;9:819018.
14. Hu B, Zou RP, Gan YW, et al. A population-based predictive model to identify patients with signet ring cell carcinoma of the stomach who are most suitable for primary tumor resection. World J Surg Oncol 2022;20:87.
15. Ye N, Bao X, Zhao X, et al. Signet-ring cell carcinoma of the duodenal bulb presenting with gastrointestinal hemorrhage: a case report and literature review. BMC Gastroenterol 2022;22:226.
16. Okamoto T, Nakamura K, Fukuda K. Successful endoscopic mucosal resection for non-ampullary duodenal signet-ring cell carcinoma. Clin J Gastroenterol 2020;13:1102-10.
17. Kinslow CJ, May MS, Kozak M, et al. Signet ring cell carcinoma of the Ampulla of Vater: outcomes of patients in the United States. HPB (Oxford) 2020;22:1759-65.
18. Mochizuki K, Kondo T, Tahara I, et al. Signet ring cell carcinoma of the non-ampullary duodenum: A case report. Pathol Res Pract 2015;211:801-4.
19. Jiang Y, Hu H, Shao X, et al. A novel web-based dynamic prognostic nomogram for gastric signet ring cell carcinoma: a multicenter population-based study. Front Immunol 2024;15:1365834.
20. Fung BM, Patel M, Patel N, et al. Signet Ring Cell Gastric Carcinoma: Clinical Epidemiology and Outcomes in a Predominantly Latino County Hospital Population. Dig Dis Sci 2021;66:1240-8.
21. Yu C, Yang J, Li H, et al. Prognostic prediction and treatment options for gastric signet ring cell carcinoma: a SEER database analysis. Front Oncol 2024;14:1473798.
22. Chu Y, Long F, Ding X, et al. The effect of surgery and metastatic risk prediction in patients with gastrointestinal tract signet-ring cell carcinoma. J Gastrointest Surg 2024;28:1234-41.
23. Ji J, Zhang X, Yuan S, et al. Survival impact of gastrectomy and chemotherapy on gastric signet ring-cell carcinoma with different metastatic lesions: A population-based study. Asian J Surg 2024;47:1769-75.
24. Liu Y, Yin W, Li X, et al. Comparative analysis of tumor

biology and prognosis in mucinous and signet-ring cell colon cancers versus classical adenocarcinoma. Front Physiol 2023;14:1199211.
25. Hugen N, Verhoeven RH, Lemmens VE, et al. Colorectal signet-ring cell carcinoma: benefit from adjuvant chemotherapy but a poor prognostic factor. Int J Cancer 2015;136:333-9.

Cite this article as: Ding J, Ye Y, Liu L. Clinicopathological characteristics and long-term prognosis of duodenal signet ring cell carcinoma: a SEER-based analysis. Transl Cancer Res 2025;14(11):7773-7789. doi: 10.21037/tcr-2025-1595