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ORIGINAL RESEARCH

A Propensity-Score Matched Analysis to Evaluate Local Treatment Modalities for Esophageal Squamous Cell Carcinoma in Over 80 years on A SEER Database

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Purpose: The aim of this study was to investigate the impact of Local treatment modalities on the survival of≥80 years older patients with squamous cell esophageal cancer, including cancer-directed surgery (CDS) or radiotherapy (RT).

Patients and Methods: Patients in the Surveillance Epidemiology and End Results (SEER) database were divided into CDS Group and RT Group D according to different Local treatment modalities. Propensity score matching (PSM) was performed to adjust for baseline differences between the two groups. Overall survival (OS) and cancer-specific survival (CSS) was calculated using the Kaplan–Meier method and compared using the Log rank test.

Results: A total of 1588 esophageal squamous cell cancer patients of ≥80 years older between 1975 and 2021 were included in the final study cohort, including 165 (10.4%) patients who underwent CDS and 1423 (89.6%) patients who received radiotherapy (RT) therapy. Univariate and multivariate analyses showed that local treatment modalities were prognostic factors for cause-specific survival (CSS) and overall survival (OS). Patients who received CDS had better CSS (HR = 0.674; 95% CI = 0.544–0.836; P < 0.000) and OS (HR = 0.717; 95% CI = 0.595–0.863; P < 0.000). In the propensity-score matched (PSM) dataset, CDS was associated with better CSS (P < 0.008) and OS (P < 0.011) for patients with ≥80 years older; Subgroup analyses showed the prognostic effect of local treatment modalities was significantly influenced by Age. Nevertheless, no differences were observed in CSS (P = 0.584) and OS (P = 0.434) for patients with ≥85 years old.

Conclusion: In conclusion, CDS was the preferred treatment for esophageal squamous cell cancer patients with 80–84 years older, and there was no difference between CDS and RT for patients with≥85 years older. This study highlight the value of different local treatments for esophageal squamous cell carcinoma over 80 years patients, especially for ≥85 years older. Further studies are needed to understand drivers of this bias and enhance equality in old patient treatment.

Keywords: elderly patients, esophageal squamous cancer, surgery, radiotherapy

Introduction

Esophageal cancer is the sixth leading global cause of cancer-related deaths.[1] The median age at diagnosis is 68 years, and more than 40% of the patients are aged 70 years or older.[2] In practice, there is still controversy on choice of treatment method for esophageal squamous cell carcinoma (ESCC) patients over 80 years old. There is limited research on the local treatment modalities or outcomes of esophageal cancer in this population, and most of it is based on the experience of small, single institutions. In this case, the use of surgery in the elderly is low and may increase postoperative complications, and older people also rarely consider definitive chemoradiotherapy, but the treatment seems to be well tolerated and the efficacy is comparable to that of younger patients.[3–6]

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Several researches suggest that histological type is associated with the efficacy of RT. One population-based study[7] showed that potentially curable esophageal adenocarcinoma cancer (EAC) (≥75 years old) had different OS between both definitive chemoradiotherapy (dCRT) or neoadjuvant chemoradiotherapy (nCRT) plus surgery, but not in ESCC (age ≥ 75 years). These differences in treatment response between patients with EAC and ESCC may be associated with tumor aggressiveness and different carcinogenesis.[8] However, studies have also shown that in elderly ESCC patients, surgery has a better OS rate than RT.[9] A meta-analysis showed that it is difficult to conclude the less efficacy of RT in elderly patients with ESCC.[10]

Most studies reporting the efficacy of local treatment for EC are focused on patients younger than 80 years old and do not differentiate between adenocarcinoma and squamous cell carcinoma based on pathological types.[5,6,9,10] Unfortunately, it is difficult to draw conclusions on local treatments in esophageal squamous cell carcinoma patients over 80 years old from previous studies. Because the lack of randomized trials, available data from small single-institution studies led to no consensus on local treatment for more than 80 years old patients with ESCC. Therefore, the most effective local treatment strategies still need to be further explored. In this regard, we used the data from the Surveillance Epidemiology and End Results (SEER) database to investigate the difference between Surgery and Radiotherapy. Furthermore, we discovered significant differences in the baseline characteristic of the studies. Thus, in this study, we performed propensity-score matched (PSM) analyses to adjust for biases from baseline characteristics of the two treatment groups.

Materials and Methods

Patient Selection in the SEER Database

Patient data were obtained from the latest version of the SEER database as released in Nov 2023 (covering 8 registries, 1973–2021), by using SEER* Stat version 8.4.3. The inclusion criteria of this study were as follows: (1) patients with esophageal squamous cell cancer were clearly diagnosed; (2) age ≥ 80 years old; (3) treatment includes chemoradiotherapy, radiotherapy alone, Surgery alone, Surgery with chemotherapy or unknown. Exclusion criteria in this study were: (1) survival time was 0 or missing; (2) patients with more than one primary tumor. The following covariates were collected from the database: age, race, marital status, primary site, grade, size and Local treatment modalities. Relevant treatment-related data included cancer-directed surgery and Radiotherapy. Duration of follow-up, and cause of death described as due to cancer-specific survival (CSS) and overall survival (OS) were also included. As the SEER database contains public data, informed consent from relevant patients for the use of the SEER database for research purposes was not required, nor was the ethical approval. This study was approved by the Hebei General Hospital Ethics Committee (Approval ID: 2025-LW-0150). This study complies with the Declaration of Helsinki. Our request for access to the SEER data was approved by the National Cancer Institute, USA (reference number 19238-Nov2021).

Statistical Analysis

The chi-squared test (or Fisher's exact test, if appropriate) was used to analyze the differences between patients grouped by categorical variables. Clinical outcomes were compared between patients treated with cancer-directed surgery (CDS) group and Radiotherapy (RT) group. Survival curves were generated using Kaplan-Meier methods, and compared by Log rank test. Univariate and multivariate Cox regression analyses were used to analyze the independent risk factors for CSS and OS. Only variables with statistical significance ($P < 0.05$) in univariate analysis were incorporated into multivariate analysis. Hazard ratios (HR) were calculated based on multivariable Cox proportional hazards models to estimate predictors of CSS and OS. All CIs were stated at the 95% confidence level. Statistical significance was set at $P < 0.05$. To adjust for differences and to minimize possible confounding effects of selection bias between CDS group and RT group for patients, we performed two PSM analyses using logistic regression at a 1:2 ratio accomplished using the nearest neighbor matching method with a caliper width equal to 0.20 standard deviation of logit of propensity score. The PSM model was based upon age, race, marital status, primary site, grade, size and surgery. The difference of each variable was considered significant if two-sided p-values less than 0.05. Statistical analyses were performed using SPSS 26.0 (SPSS Inc., Chicago, IL) and R software (version 3.5.1).

Results

Baseline Characteristics in the Entire Population

In the unmatched database, a total of 1588 patients met our inclusion criteria and were included in our final analysis. The median follow-up time was 147.0 months (range: 103.8–190.2 months) in CDS Group and 169.0 months (range: 90.5–247.5 months) in RT Group. Table 1 summarizes the characteristics of the study population. A total of 165 (10.4%) patients underwent CDS and 1423 (89.6%) patients received RT treatment. Significant differences between two treatment groups were recorded regarding patient characteristics. As shown in Table 1, it was investigated that significant

Table 1 Characteristics of Patients

Variable	CDS		RT		P value
	n=165	(%)	n=1423	(%)	
Age					
80-84	125	75.80	847	59.50	0.000
≥85	40	24.20	576	40.50	
Sex					
Male	90	54.50	776	54.50	0.998
Female	75	45.50	647	45.50	
Marital status					
Married	76	46.10	583	41.00	0.209
Single	89	53.90	840	59.00	
Race					
White	138	83.60	1137	79.90	0.509
Asian	19	11.50	195	13.70	
Other	8	4.80	91	6.40	
Location					
Cervical	6	3.60	85	6.00	0.355
Thoracic	141	85.50	1175	82.60	
Abdomen	1	0.60	3	0.20	
Overlap	10	6.10	66	4.60	
Unknown	7	4.20	94	6.60	
Size					
1-3cm	66	40.00	240	16.90	0.000
4-6cm	42	25.50	304	21.40	
7-9cm	13	7.90	193	13.60	
≥10cm	2	1.20	42	3.00	
Unknown	42	25.50	644	45.30	
Grade					
I	11	6.70	77	5.40	0.032
II	70	42.40	510	35.80	
III	63	38.20	510	35.80	
IV	3	1.80	21	1.50	
Unknown	18	10.90	305	21.40	
Stage					
Local	60	36.40	460	32.30	0.000
Regional	79	47.90	415	29.20	
Distant	8	4.80	226	15.90	
Unknown	18	10.90	322	22.60	
Chemotherapy					
Yes	2	1.20	584	41.00	0.000
No/ Unknown	163	98.80	839	59.00	

Abbreviations: CDS, cancer-directed surgery; RT, radiotherapy.

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differences were found among the Age, Grade, Stage, Tumor Size and Chemotherapy. All of them had statistical difference ($P < 0.05$) except Sex, Race, Location and marital status ($P>0.05$).

Analysis of Prognostic Factors

In the dataset, univariate analysis showed that age, sex, tumor size, grade, stage, chemotherapy and local treatment modalities were prognostic factors that affected OS and CSS ($P < 0.05$; Tables 2 and 3). Marital status and race

Table 2 Univariate and Multivariate Analysis of Overall Survival

Variable	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
Age						
≥85	1			1		
80-84	0.848	0.764–0.941	0.002	0.873	0.784–0.971	0.013
Sex						
Female	1			1		
Male	1.235	1.116–1.368	0.000	1.210	1.08–1.344	0.000
Marital status						
Married	1			–		
Single	1.067	0.963–1.183	0.214	–	–	–
Race						
White	1			–		
Asian	1.043	0.898–1.212	0.583	–	–	–
Other	1.106	0.896–1.364	0.348	–	–	–
Location						
Overlap	1			–		
Cervical	0.775	0.569–1.055	0.105	–	–	–
Thoracic	0.803	0.635–1.016	0.068	–	–	–
Abdomen	0.780	0.285–2.136	0.628	–	–	–
Unknown	0.826	0.611–1.118	0.215	–	–	–
Size						
1-3cm	1			1		
4-6cm	1.605	1.366–1.886	0.000	1.525	1.29–1.797	0.000
7-9cm	1.935	1.611–2.324	0.000	1.682	1.393–2.301	0.000
≥10cm	2.251	1.623–3.122	0.000	1.818	1.304–2.534	0.000
Unknown	1.785	1.548–2.058	0.000	1.606	1.382–1.866	0.000
Grade						
IV	1			1		
I	0.412	0.261–0.650	0.000	0.471	0.298–0.745	0.001
II	0.504	0.334–0.759	0.001	0.581	0.385–0.878	0.010
III	0.530	0.352–0.798	0.002	0.557	0.369–0.841	0.005
Unknown	0.496	0.327–0.752	0.001	0.531	0.349–0.807	0.003
Stage						
Distant	1			1		
Local	0.535	0.456–0.628	0.000	0.521	0.442–0.615	0.000
Regional	0.600	0.510–0.705	0.000	0.640	0.543–0.755	0.000
Unknown	0.790	0.667–0.936	0.000	0.651	0.545–0.779	0.000
Chemotherapy						
Yes	1			1		
No/ Unknown	1.590	1.431–1.771	0.000	1.797	1.598–2.021	0.000
Local treatment modalities						
RT	1			1		
CDS	0.762	0.645–0.900	0.001	0.717	0.595–0.863	0.000

Abbreviations: HR, hazard ratio; CI, confidence interval; CDS, cancer-directed surgery; RT, radiotherapy.

Table 3 Univariate and Multivariate Analysis of Cause-Specific Survival

Variable	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
Age						
≥85	1			1		
80-84	0.848	0.755–0.952	0.005	0.877	0.779–0.988	0.031
Sex						
Female	1			1		
Male	1.181	1.054–1.324	0.004	1.149	1.021–1.292	0.021
Marital status						
Married	1			–		
Single	1.080	0.963–1.212	0.189	–	–	–
Race						
White	1			–		
Asian	1.050	0.889–1.241	0.564	–	–	–
Other	1.106	0.875–1.399	0.400	–	–	–
Location						
Overlap	1			–		
Cervical	0.653	0.465–0.916	0.014	–	–	–
Thoracic	0.730	0.570–0.936	0.013	–	–	–
Abdomen	0.758	0.238–2.413	0.639	–	–	–
Unknown	0.693	0.495–0.966	0.031	–	–	–
Size						
1-3cm	1			1		
4-6cm	1.685	1.400–2.028	0.000	1.563	1.296–1.885	0.000
7-9cm	2.079	1.690–2.559	0.000	1.753	1.417–2.168	0.000
≥10cm	2.256	1.565–3.252	0.000	1.718	1.186–2.490	0.000
Unknown	1.865	1.582–2.198	0.000	1.655	1.394–1.964	0.000
Grade						
IV	1			–		
I	0.449	0.275–0.734	0.001	–	–	–
II	0.486	0.313–0.754	0.001	–	–	–
III	0.515	0.332–0.798	0.003	–	–	–
Unknown	0.487	0.311–0.761	0.002	–	–	–
Stage						
Distant	1			1		
Local	0.508	0.426–0.604	0.000	0.499	0.417–0.598	0.000
Regional	0.567	0.475–0.676	0.000	0.624	0.521–0.748	0.000
Unknown	0.726	0.603–0.875	0.001	0.588	0.483–0.715	0.000
Chemotherapy						
Yes	1			1		
No/ Unknown	1.639	1.452–1.849	0.000	1.825	1.601–2.080	0.000
Local treatment modalities						
RT	1			1		
CDS	0.706	0.580–0.860	0.001	0.674	0.544–0.836	0.000

Abbreviations: HR, hazard ratio; CI, confidence interval; CDS, cancer-directed surgery; RT, radiotherapy.

were not associated with OS (P > 0.05; Table 2). Location affected CSS (P < 0.05; Table 3), but not OS (P > 0.05; Table 2).

Multivariate analysis showed that age, sex, tumor size, stage, chemotherapy and local treatment modalities were prognostic factors that affected OS and CSS (P < 0.05; Tables 2 and 3). Grade affected OS (P < 0.05; Table 2), but not

CSS (P > 0.05; Table 3). Patients who received CDS treatment had better OS (HR = 0.717; 95% CI: 0.595–0.863; P < 0.05; Table 2) and CSS (HR = 0.674; 95% CI: 0.544–0.836; P < 0.05; Table 3).

Impact of Local Treatment Modalities on Survival

In the original cohort, according to the survival curve, the median OS of CDS was 11.0 months (95% CI:8.2–13.8 months), which was significantly better than that of RT group (8.0 months) (95% CI: 7.4–8.6 months) (P < 0.05) (Figure 1a). The median CSS of CDS was 16.0 months (95% CI:12.3–19.7 months), which was significantly better than that of RT (10.0 months) (95% CI:9.3–10.7months) (P < 0.05) (Figure 1b). Because there were both significant differences in the baseline characteristic of two groups, we performed PSM analyses at a 1:2 ratio to erase significant difference of each variable, respectively (Table 4). The 1:2 matching for CDS versus RT resulted in a sample size of 379 patients. In the matched dataset, we obtained similar results: the median OS of CDS was 10.0 months, which was significantly better than that of RT group (8.0 months) (P < 0.05) (Figure 1c). The median CSS of CDS was 13.0 months, which was significantly better than that of RT (10.0 months) (P < 0.05) (Figure 1d).According to subgroup analysis, as shown in Tables 5 and 6, CDS was associated with better OS and CSS in In the 80–84 age group (P < 0.05) (Figure 2a–c respectively); nevertheless, no differences were observed in OS and CSS according to different local treatment modalities in over 85 years old group (P>0.05) (Figure 2b–d, respectively).

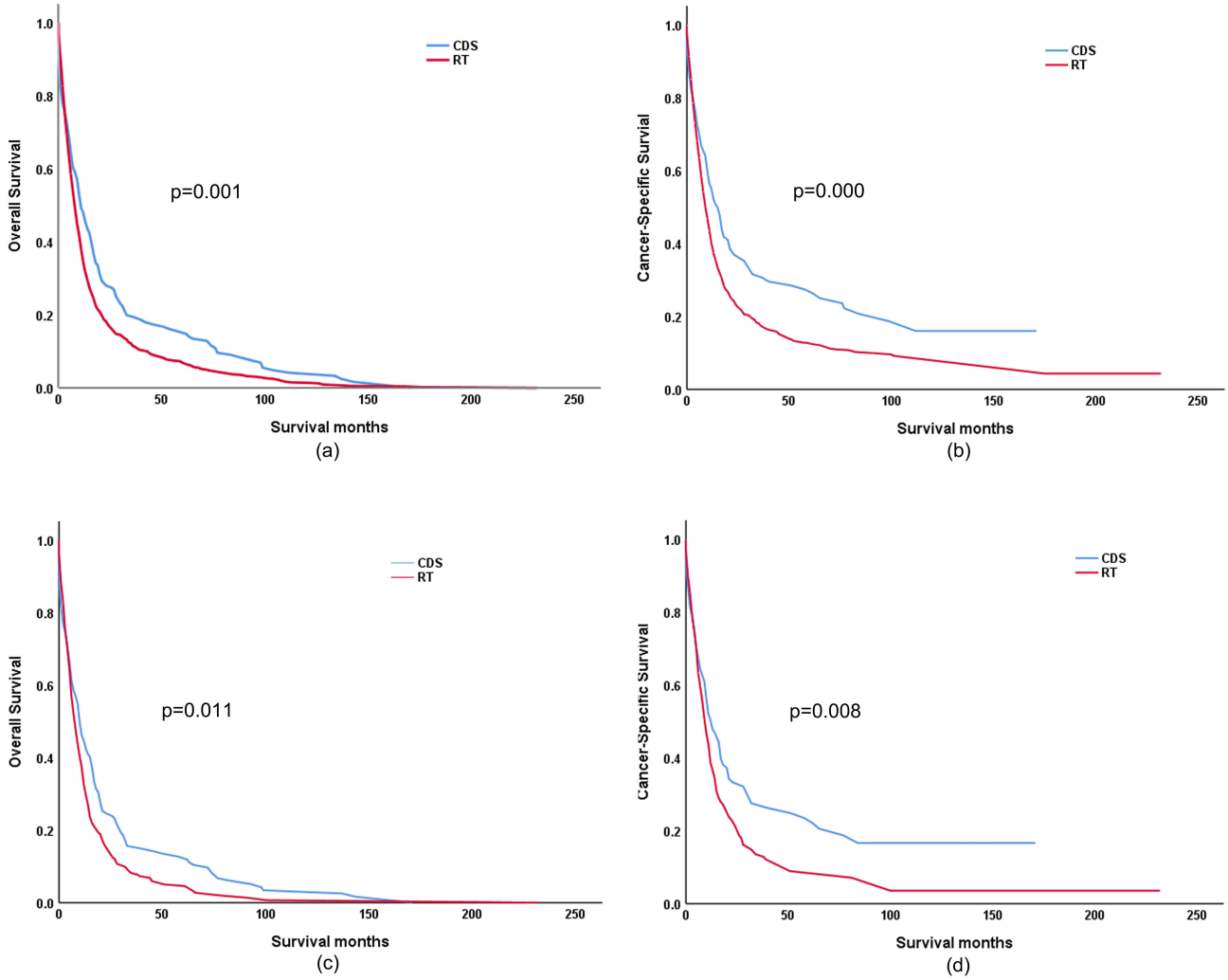

Figure 1 Overall survival and Cancer-specific survival of esophageal squamous cancer patients with ≥80 years older before and after PSM. OS before PSM (**a**), CSS before PSM (**b**), OS after PSM (**c**) and CSS after PSM (**d**) with different local treatment modalities.

Table 4 Characteristics of PSM Cohorts for Patients

Variable	CDS		RT		P value
	n=139	(%)	n=240	(%)	
Age					
80-84	99	71.20	157	65.40	0.245
≥85	40	28.80	83	34.60	
Sex					
Male	73	52.50	137	57.10	0.389
Female	66	47.50	103	42.90	
Marital status					
Married	58	41.70	101	42.10	0.946
Single	81	58.30	139	57.90	
Race					
White	119	85.60	190	79.20	0.296
Asian	13	9.40	32	13.30	
Other	7	5.00	18	7.50	
Location					
Cervical	5	3.60	18	7.50	0.485
Thoracic	116	83.50	198	82.50	
Abdomen	1	0.70	1	0.40	
Overlap	10	7.20	11	4.60	
Unknown	7	5.00	12	5.00	
Size					
1-3cm	48	34.50	75	31.30	0.797
4-6cm	34	24.50	62	25.80	
7-9cm	13	9.40	17	7.10	
≥10cm	2	1.40	6	2.50	
Unknown	42	30.20	80	33.30	
Grade					
I	9	6.50	18	7.50	0.263
II	67	48.20	87	36.30	
III	42	30.20	91	37.90	
IV	3	2.20	6	2.50	
Unknown	18	12.90	38	15.80	
Stage					
Local	55	39.60	93	38.80	0.964
Regional	58	41.70	98	40.80	
Distant	8	5.80	17	7.10	
Unknown	18	12.90	32	13.30	
Chemotherapy					
Yes	2	1.40	10	4.20	0.224
No/Unknown	137	98.60	230	95.80	

Abbreviations: CDS, cancer-directed surgery; RT, radiotherapy.

Discussion

In the modern elderly patient population with esophageal squamous cell cancer, our research results indicate significant differences in treatment utilization and related outcomes based on demographic and tumor characteristics. Treatment outcomes are significantly influenced by age, gender, tumor size, stage, grade. Local treatment modalities and chemotherapy also affect utilization rates in specific situations. As the aggressiveness of treatment increases from definitive radiotherapy to surgical treatment of the disease, survival rates gradually improve.

In the elderly population, age is one of the strongest predictors of treatment utilization and survival. More than 80 years old patients are more likely to not receive treatment in non-definitive therapy, while the likelihood of receiving

Table 5 Overall Survival of Subgroups Analysis for Local Treatment Modalities

Variable	CDS			RT			P
	n	Median OS	95% CI	n	Median OS	95% CI	
All	139	10	7.6–12.4	240	8	6.6–9.4	0.011
Age							
80-84	99	11	6.2–15.8	157	7	5.1–8.9	0.015
≥85	40	9	4.2–13.8	83	9	6.6–11.4	0.434
Sex							
Male	73	7	4.5–9.5	137	7	5.5–8.5	0.404
Female	66	15	11.1–18.9	103	10	7.4–12.6	0.018
Marital status							
Married	58	8	5.3–10.7	101	8	5.8–10.2	0.077
Single	81	11	8.1–13.9	139	8	6.1–9.9	0.052
Race							
White	119	10	7.1–12.9	190	8	6.3–9.7	0.029
Asian	13	10	0.0–20.9	32	9	5.7–12.3	0.794
Other	7	30	6.6-53	18	3	0.5–5.5	0.009
Location							
Cervical	5	9	0.0–26.2	18	6	0.5–11.5	0.474
Thoracic	116	11	8.8–13.2	198	8	6.6–9.4	0.020
Abdomen	1	98	–	1	1	–	–
Overlap	10	3	0.0–6.1	11	12	4.4–19.6	0.195
Unknown	7	31	0.0–66.9	12	5	0.0–13.5	0.086
Size							
1-3cm	48	20	10.7–29.3	75	10	7.5–12.5	0.011
4-6cm	34	6	3.6–8.4	62	7	4.8–9.2	0.334
7-9cm	13	8	0.0–16.2	17	7	4.6–9.4	0.918
≥10cm	2	0	–	6	12	7.5–16.5	0.008
Unknown	42	10	6.4–13.6	80	7	5.4–8.6	0.520
Grade							
I	9	2	0.0–4.9	18	9	6.0–12.0	0.940
II	67	10	6.9–13.1	87	9	6.2–11.8	0.117
III	42	10	3.6–16.4	91	7	5.4–8.6	0.091
IV	3	2	0.0–5.2	6	5	0.0–13.4	0.721
Unknown	19	11	0.0–23.5	38	8	4.0–12.0	0.163
Stage							
Local	55	16	7.0–25.0	93	9	7.3–10.7	0.001
Regional	58	9	5.3–12.7	98	7	5.6–8.4	0.186
Distant	8	7	0.0–19.5	17	6	3.5–8.5	0.549
Unknown	18	5	0.8–9.2	32	9	5.5–12.5	0.199
Chemotherapy							
Yes	2	5	–	10	16	4.4–27.6	0.073
No/Unknown	137	11	8.3–13.7	230	8	6.7–9.4	0.008

Abbreviations, CDS, cancer-directed surgery; RT, radiotherapy.

triple therapy and individual esophagectomy in definitive therapy is much lower. These differences may be a combination of patient related factors, physician bias, and clinical reality. In theory, as age increases, the comorbidity rate should increase and physiological reserves should decrease, leading to a decrease in tolerance to aggressive treatment with age. Towards older adults, stem cell reserves and the presence of comorbidities that affect drug absorption and/or metabolism. In addition, esophagectomy is associated with a higher perioperative mortality rate in elderly people. In a large retrospective study evaluating the safety of esophagectomy in elderly patients, the surgical mortality rate significantly

Table 6 Cause-Specific Survival of Subgroups Analysis for Local Treatment Modalities

Variable	CDS			RT			P
	n	Median CSS	95% CI	n	Median CSS	95% CI	
All	139	13	8.5–17.5	240	10	8.3–11.7	0.008
Age							
80-84	99	16	11.3–20.7	157	9	7.0–11.1	0.006
≥85	40	12	5.0–19.0	83	11	8.2–13.8	0.584
Sex							
Male	73	10	6.9–13.1	137	9	7.1–10.9	0.325
Female	66	17	12.0–22.1	103	11	8.5–13.5	0.016
Marital status							
Married	58	10	3.1–16.9	101	9	6.6–11.4	0.066
Single	81	13	8.5–17.5	139	10	7.9–12.1	0.044
Race							
White	119	12	7.6–12.4	190	10	8.0–12.0	0.029
Asian	13	14	4.0–24.0	32	9	4.7–13.3	0.636
Other	7	30	0.0–81.0	18	7	0.0–14.9	0.023
Location							
Cervical	5	17	0.0–40.3	18	6	0.5–11.5	0.452
Thoracic	116	12	8.0–16.1	198	10	8.3–11.7	0.026
Abdomen	1	–	–	1	–	–	–
Overlap	10	3	0.0–6.1	11	12	1.0–23.0	0.232
Unknown	7	84	0.0–186.3	12	5	0.0–13.5	0.076
Size							
1-3cm	48	40	2.0–78.0	75	12	7.3–16.7	0.001
4-6cm	34	7	4.3–9.7	62	9	6.4–11.6	0.525
7-9cm	13	8	0.0–16.2	17	9	4.4–13.6	0.827
≥10cm	2	0		6	12	7.5–16.5	0.008
Unknown	42	11	7.8–14.2	80	8	5.3–10.7	0.438
Grade							
I	9	5	0.0–10.1	18	9	6.1–11.9	0.927
II	67	13	6.9–19.1	87	11	8.8–13.2	0.118
III	42	12	5.1–18.9	91	9	6.9–11.1	0.167
IV	3	2	0.0–5.2	6	8	0.0–21.7	0.834
Unknown	19	30	0.0–61.0	38	10	5.1–15.0	0.069
Stage							
Local	55	40	6.0-74	93	10	7.4–12.6	0.000
Regional	58	11	7.6–14.4	98	8	5.6–10.4	0.288
Distant	8	13	0.0–28.4	17	6	3.5–8.5	0.354
Unknown	18	7	1.0–13.0	32	15	11.4–18.6	0.042
Chemotherapy							
Yes	2	5	–	10	17	10.5–23.5	0.073
No/Unknown	137	13	9.3–16.7	230	9	7.4–10.6	0.006

Abbreviations: CDS, cancer-directed surgery; RT, radiotherapy.

increased with age (8.8% for 65–69 years old, 13.4% for 70–79 years old, and 19.9% for those over 80 years old).[11] In our analysis, surgery significantly prolonged OS and CSS compared to RT in ≥ 80 years age group. Although baseline characteristic of patients may affect these findings, we do see consistent improvement in matching cohorts with more aggressive treatment. However, surgery was not associated with a better OS in age ≥85 years groups compared to RT in subgroup analysis. However, in properly selected individuals, the incidence rate and mortality of esophagectomy are comparable to those of patients in their 80s.[12,13]

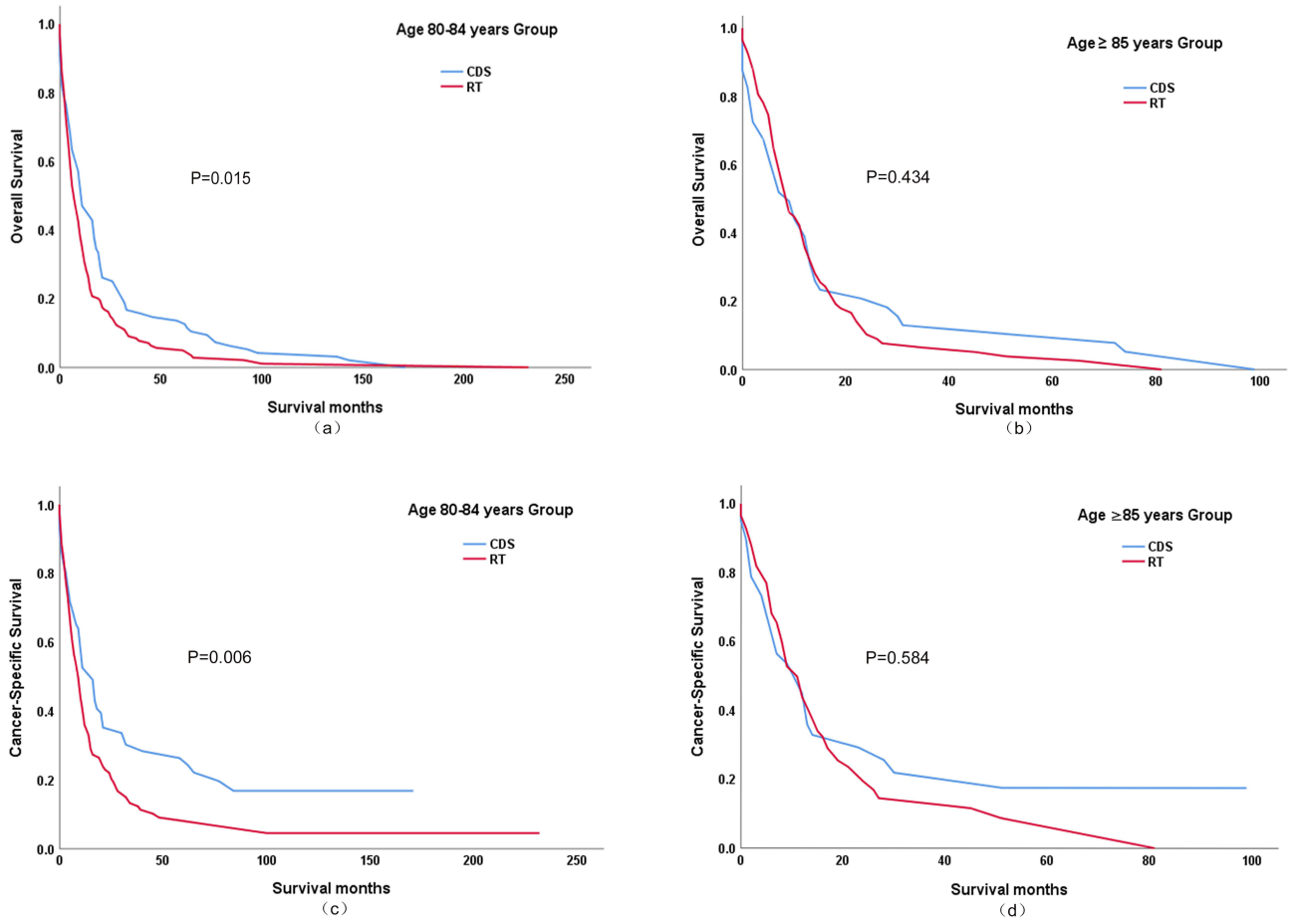

Figure 2 Overall survival and Cancer-specific survival of esophageal squamous cancer patients with 80–84 years and ≥85 years older after PSM. OS with 80–84 years (**a**) and ≥85 years older (**b**), CSS with 80–84 years (**c**) and ≥85 years older(**d**) with different local treatment modalities.

Endoscopy is used for staging esophageal cancer patients, especially T staging, and can be performed noninvasively. However, elderly patients have more preexisting comorbidities, which are contraindications for this surgery. Therefore, in this study, we used tumor Size and SEER staging instead of TNM staging. Before using endoscopic staging in EC, tumor Size (1–3cm,4–6cm,7–9cm, ≥10cm), is used to predict patient prognosis.[14] Several studies have identified that tumor Size is an important prognostic factor for esophageal cancer (EC) in different treatment strategies for young patients.[15–17] Similarly, our research findings indicate that tumor size is also a prognostic factor for elderly patients.

Gender is also a predictive factor for the utilization rate and survival rate of esophageal cancer treatment. The results also described esophageal cancer, in which male patients had lower long-term survival rates after surgery.[18–20] A nationwide study in Sweden reported a prognostic advantage for female patients with esophageal squamous cell carcinoma (ESCC) both after either curative surgery or dCRT, while no such difference was observed for adenocarcinoma (AC).[21] Another study, including patients from a variety of European and North-American centers, highlights that survival was improved for women in the AC group, whereas this difference was not confirmed in squamous cell cancer.[22] In the current analysis, the predominant subtype of SCC in women has improved survival rates. Although differences in mortality caused by concurrent diseases may be a contributing factor, gender differences in disease progression and treatment response are an unexplored possibility. A possible biological mechanism for a sex difference is estrogenic influence, which could inhibit cancer cell growth.[23,24] Healthcare-seeking patterns, socioeconomic and lifestyle factors might also differ between the sexes, with women more readily and more often using health resources available to them, compared with men. Further research is needed to delve deeper into this hypothesis.

Univariate and multivariate analysis showed that chemotherapy (CT) associated with good prognosis. However, subgroup analysis suggested that CDS for patients did not improve the OS and CSS over RT in CT group. Although the

chemotherapy and radiotherapy regimen not recorded in this study, we should note that elderly patients with combined therapy do not tend to improve OS compared to younger patients. *Jingu* et al reported that concurrent chemotherapy with radiotherapy did not have significant OS benefit over radiotherapy alone for esophageal cancer in patients aged 80 years or older, and the chemotherapeutic regimens were platinum based dual drugs (n=62), and single chemotherapy drug (n=17).[25] *Ji* et al reported that CRT with S-1 (≥80 years: 37 (24.8%)) provided significant benefits over radiotherapy alone (≥80 years: 39 (26.2%)) in older patients with EC in a Phase III randomized clinical trial.[26] The chemotherapy regimen and combined with CDS/RT can be considered in the future to improve the OS of elderly patients with EC.

There were some limitations to our study. First, In practical clinical treatment, ≥80 years patients with ESCC who were assessed as not tolerating chemotherapy or unwilling to undergo chemotherapy.[27,28] It should be noted that, due to the lack of medical information in the SEER database, we were unable to obtain details of chemotherapy. Potential chemotherapy may influence survival, which lead to biased results. Second, in our study, patients received different doses of radiotherapy, which may have led to some deviations in the survival and safety of patients. In addition, we did not comprehensively assess the health status and quality of life after treatment in elderly patients, which may be a key factor in influencing whether patients can complete treatment, and can better assess the safety of local treatment Local treatment modalities. We were unable to evaluate toxicities, because of lack of information in the registry.

Conclusion

In conclusion, our study provided creditable evidence for characteristics and outcome for ESCC patients aged ≥ 80 years old based on large, population-based registry. Our study suggested that ESCC patients aged ≥ 80 years old benefit from CDS only if the cancer is in localized/regional stage, but not in ≥85 years older in subgroup analysis. However, the limitations of this study must be acknowledged; therefore, more large-scale prospective randomized clinical trials are warranted to investigate the effect of local treatment on over 80 years old patients with ESCC.

Statement of Ethics

This study was approved by the Hebei General Hospital Ethics Committee (Approval ID: 2025-LW-0150). All procedures were performed in accordance with the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The author(s) report(s) no conflicts of interest in this work.

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