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Original Article

Efficacy and Safety of Chemoradiotherapy with Carboplatin and Paclitaxel in Older Adults with Esophageal Cancer

Chung-Hao Ku[1], Ming-Mo Hou[1], Chen-Kan Tseng[2], Kun-Yun Yeh[3], Chang-Hsien Lu[4], Wen-Chi Chou[1]*

[1]Department of Hematology and Oncology, Chang Gung Memorial Hospital at Linkou and College of Medicine, Chang Gung University, Taoyuan, Taiwan
[2]Department of Radiation Oncology, Chang Gung Memorial Hospital at Linkou and College of Medicine, Chang Gung University, Taoyuan, Taiwan
[3]Department of Oncology, Chang Gung Memorial Hospital, Keelung, Taiwan
[4]Department of Oncology, Chang Gung Memorial Hospital, Chiayi, Taiwan

Abstract

Background: Concurrent chemoradiotherapy (CCRT) using the paclitaxel/carboplatin regimen, as established in the CROSS study, has become a standard neoadjuvant treatment prior to surgery for patients with locally advanced esophageal cancer. However, its impact on older patients requires further study to guide clinical decision making. **Materials and Methods:** This retrospective analysis included 87 patients with locally advanced esophageal cancer treated at three institutes in Taiwan between 2016 and 2017. All patients received CCRT comprising weekly carboplatin and paclitaxel combined with intensity-modulated or arc radiotherapy. Survival, treatment efficacy, adverse events, and complications were assessed and stratified by age groups (<65 vs. ≥65, <70 vs. ≥70, and <75 vs. ≥75 years). **Results:** The 1- and 2-year survival rates were 71.0% and 55.5%, respectively, for patients <65 years, and 72.2% and 61.0% for patients aged ≥65 years, with no significant differences across age groups. The objective response rate was 76%, consistent across all age subgroups. Surgical resection was performed in 49% of the patients, achieving a 77% complete (R0) resection rate across age groups. Toxicities were prevalent but not age-specific in most cases, with 75% of the patients experiencing adverse events. Hematological toxicities were common, with leukopenia (32%) and anemia (17%) being the most frequent. Nonhematological toxicities included mucositis (23%) and infection (17%). Older patients had a higher incidence of hypertension during treatment (≥70 years: 23% vs. 3%, $P = 0.022$). Emergency visits and hospitalizations occurred in 30% and 24% of the patients, respectively, during CCRT, without significant age differences. **Conclusion:** CCRT appears to be a feasible treatment option for selected patients with esophageal cancer, including older adults, with good performance status and preserved organ function.

Keywords: Chemoradiotherapy, geriatric, outcome, safety profile, tolerance

Introduction

Esophageal cancer is a highly aggressive malignancy, ranked as the 17th most common newly diagnosed cancer and the

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Address for correspondence: Dr. Wen-Chi Chou, Department of Hematology and Oncology, Chang Gung Memorial Hospital, No. 5, Fu-Hsing Street, Kwei-Shan Shiang, Taoyuan, Taiwan.
E-mail: wenchi3992@yahoo.com.tw

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8th leading cause of cancer-related mortality in the United States.[1] It is particularly prevalent in Taiwan, where it was the 6th most common newly diagnosed cancer and the 5th leading cause of cancer-related death in males in 2022.[2] The median age at diagnosis for esophageal cancer is 68 years in the US, with over 63% of patients being 65 years or older at the time of diagnosis.[3] In Taiwan, the median age at diagnosis is 60 years for males and 63 years for females, with over 32% of patients being 65 years or older at the time of diagnosis.[2] Given the significant proportion of older individuals (defined in this study as age ≥65 years) affected by esophageal cancer, it is crucial to investigate the impact of antitumor therapies on this patient population, as they may face unique challenges and treatment-related side effects that could influence their health-related quality of life and overall survival (OS).

Concurrent chemoradiotherapy (CCRT) using paclitaxel/carboplatin (CROSS regimen) has become a standard neoadjuvant treatment prior to surgery for patients with locally advanced esophageal cancer, following the results of the CROSS trial, which demonstrated improved survival compared to surgery alone.[4] Specifically, this regimen was shown to increase the complete resection rate from 69% with surgery alone to 92% with combined therapy, while also reducing the risk of death by 34% and the risk of relapse by 42%. Carboplatin is preferred over the conventional cisplatin regimen due to its lower incidence of neurotoxicity and easier administration in the outpatient setting, which can be particularly advantageous for older patients.[5,6] However, the CROSS study enrolled patients aged 18–75 years, and the specific impact of this regimen on an exclusively older patient population remains unclear.[4,7-15]

Assessing the efficacy and safety profile of older cancer patients is crucial, as they may experience specific toxicities and challenges that could negatively impact their survival outcomes.[16-18] This study investigated the tolerability, safety, and effectiveness of CCRT with carboplatin and paclitaxel in older adults with esophageal cancer, to help develop better treatment approaches for this patient group.

Materials and Methods

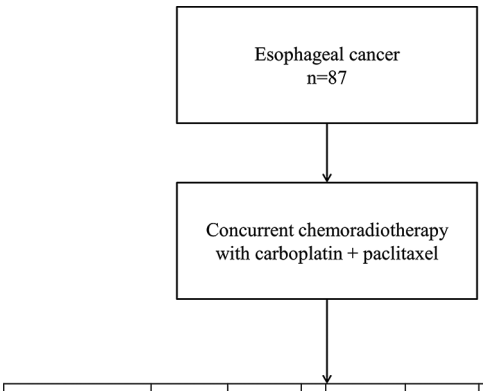
Patient selection

Patients were recruited consecutively between August 2016 and December 2017 from three medical institutes in Taiwan. The inclusion criteria were: patients aged 20 years or older with histologically confirmed esophageal cancer, who had locally advanced disease, and were eligible for CCRT as the first-line antitumor treatment. All patients who met the inclusion criteria and received CCRT as the first-line treatment during the study period were included. No additional exclusion criteria were applied. Locally advanced disease was defined as any nonmetastatic tumor from the cervical esophagus, with a tumor classification of ≥T2, or any regional nodal-positive tumor. Tumor staging was conducted according to the 7th edition of the American Joint Committee on Cancer staging system.[19] This study was designed as a prospective cohort with retrospective data analysis. The study was conducted in accordance with the Declaration of Helsinki. The study protocol and data collection process were approved by the Institutional Review Board of Chang Gung Memorial Hospital on September 12, 2016 (Approval No. 201600916B0), before the retrieval and analysis of patient data. A written informed consent was obtained from all subjects. Figure 1 shows the age subgroup allocation in this study.

Preoperative concurrent chemoradiotherapy and toxicity recording

All eligible participants underwent CCRT according to the CROSS study protocol.[4] Specifically, they received intensity-modulated or arc technique radiotherapy at a dose of 1.8 Gy per fraction, for a total of 23 fractions (41.4 Gy) to the tumor bed and regional lymphatics. An additional localized boost of 5.0–23.4 Gy was administered to the primary tumor and involved lymph node areas in patients who either did not undergo surgical resection or had positive pathological lymph node metastases after surgery. Concurrently, the participants were administered a chemotherapy regimen with carboplatin (area under the curve of 2 mg/ml/min) and paclitaxel (50 mg/m^2 of body surface area) on a weekly basis for up to 5 weeks. Following completion of CCRT, the patients were encouraged to undergo radical surgery within 4–6 weeks. For those who did not undergo surgical resection or had positive lymph node metastases after surgery, additional localized radiotherapy with 2340 cGy over 13 fractions was provided to the primary tumor and the involved lymph node area. In this real-world study, there were no protocol-defined criteria for chemotherapy or radiotherapy dose modifications**.** Treatment adjustments were made based on clinical judgment, with physicians modifying doses according to patient tolerance, observed toxicities, and overall compliance.

Tumor response following CCRT was evaluated according to RECIST version 1.0**,** using contrast-enhanced computed



Age, years	<65	≥65	<70	≥70	<75	≥75
n	68	19	74	13	78	9
%	78	22	85	15	90	10

Figure 1: Age subgroups allocation in this study

tomography (CT) and esophagogastroduodenoscopy (EGD). These assessments were conducted within 4 weeks after completing CCRT (41.4 Gy) to determine clinical objective response. Treatment response was primarily evaluated by experienced gastrointestinal radiologists using serial CT imaging, based on changes in tumor thickness and lymph node size. In cases where the primary tumor was difficult to assess by imaging alone, endoscopic evaluation and clinical judgment were also incorporated. This methodology is consistent with our prior study.[8]

The patients were followed regularly postoperatively or after definitive CRT. Follow-up visits were scheduled every 3–6 months during the first 2 years and every 6–12 months thereafter. Standard follow-up assessments typically included a detailed physical examination, chest and abdominal CT scans, and EGD. The precise intervals and types of examinations were adjusted according to clinical discretion based on the condition of the patient and judgment of the treating physician.

Toxicity profiles were assessed using the National Cancer Institute's Common Terminology Criteria for adverse events version 3.0.[20] Grade III or higher toxicity was defined as a serious adverse event (sAE). Emergency room (ER) visits and unplanned hospitalizations were recorded independently; however, they often coincided with sAEs. For example, patients with Grade ≥3 neutropenic fever, mucositis, or infections were frequently classified into both sAE and complication categories when such events led to ER visits or hospital admissions.

Complications of CCRT were defined as incomplete treatment, ER visits, or unplanned hospitalization during the CCRT period. Patients who received <90% of the protocol-specified radiotherapy dose or fewer than five chemotherapy administrations were considered to have had incomplete radiotherapy or chemotherapy, respectively.[8] All enrolled patients were followed up until May 31, 2019, or until death. Dates of tumor recurrence or death were verified using data from the Institutional Cancer Registry and the National Registry of Death database in Taiwan to ensure accuracy of OS outcomes. Survival time was determined from the first date of CCRT until death or until the last date on which the patient was known to be alive.

Statistical analysis

Descriptive statistics were used to summarize patient and tumor characteristics. The Kruskal–Wallis test for continuous and ordinal variables and the Chi-square test for categorical variables were used for in-group comparisons. Survival outcomes were evaluated using the Kaplan–Meier method, and log-rank tests were used to determine significant differences between survival curves. A Cox regression model was applied to estimate the hazard ratio for variables associated with OS. Statistical analyses were conducted using SPSS 17.0 software (SPSS Inc., Chicago, IL, USA). All statistical assessments were two-sided, and $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

Table 1 provides a detailed summary of the baseline demographics and clinical characteristics of the 87 patients included in the study, stratified by age subgroups. The median age of the study cohort was 56 years, with a range from 28 to 82 years. Patients aged ≥65, ≥70, and ≥75 years accounted for 22%, 15%, and 10% of the cohort, respectively. The overall study population was predominantly male, although the proportion of males slightly decreased with advancing age. The median body mass index remained consistent at 22.4 kg/m^2 across all age groups, and most participants were married. There were no significant differences in body mass index, marital status, or educational attainment among the age subgroups.

The rates of smoking (87%) and alcohol consumption (92%) were high, with a significantly lower alcohol consumption rate among the patients aged ≥75 years ($P = 0.02$). Tumor characteristics, including the tumor being located predominantly in the middle or lower esophagus and histological type overwhelmingly being squamous cell carcinoma, were comparable across all age groups. Most of the patients presented with stage III disease, and the Charlson Comorbidity Index scores were evenly distributed, indicating no significant differences in comorbidities among the age subgroups. Most participants had good functional status, with 98% categorized as Eastern Cooperative Oncology Group performance status 0 or 1.

Impact of age on survival

The median follow-up period was 21.5 months (range: 6.8–29.6 months), and 33 of the 87 patients (37.9%) had died by the last follow-up date (May 31, 2019). The 1- and 2-year OS rates were 71.2% and 56.9%, respectively. The survival outcomes were comparable across the younger and older age groups. The 1-year survival rates were 71.0% for patients aged <65 years and 72.2% for those aged ≥65 years [log-rank $P = 0.81$, Figure 2a]. Similarly, the 1-year survival rates were 73.4% for patients aged <70 years and 58.3% for those aged ≥70 years [log-rank $P = 0.42$, Figure 2b] and 73.4% for patients aged <75 years and 50.0% for those aged ≥75 years [log-rank $P = 0.22$, Figure 2c]. These findings suggested that age did not significantly impact the survival outcomes in this patient population.

Concurrent chemoradiotherapy efficacy

The efficacy of CCRT was consistent across the age groups. As shown in Table 2, the overall objective response rate (ORR) was 76%, and the ORRs were similar across all age subgroups. The patients <65 years had an ORR of 75%, while those ≥65 years had an ORR of 79%. This difference was not statistically significant. Similarly, no significant differences were observed between the patients younger and older than 70 years, or between those younger and older than 75 years.

Approximately half of the patients ($n = 43$, 49%) underwent surgical resection after completing CCRT. The percentage

Table 1: Baseline demographics and characteristics

Variables, *n* (%)	All (*n*=87)	Age <65 (*n*=68)	Age ≥65 (*n*=19)	*P*	Age <70 (*n*=74)	Age ≥70 (*n*=13)	*P*	Age <75 (*n*=78)	Age ≥75 (*n*=9)	*P*
Sex				0.26			0.36			0.08
Male	76 (87)	60 (88)	16 (84)		66 (89)	10 (77)		70 (90)	6 (67)	
BMI, median (range)	22.4 (15.9–31.6)	22.4 (15.9–31.6)	22.4 (16.9–27.3)	0.49	22.5 (15.9–31.6)	19.6 (16.9–27.3)	0.15	22.5 (15.9–31.6)	19.6 (16.9–27.3)	0.15
Marriage										
Yes	72 (83)	55 (81)	17 (90)	0.26	61 (82)	11 (85)	0.83	65 (83)	7 (78)	0.71
No	15 (17)	13 (19)	2 (10)		13 (18)	2 (15)		13 (17)	2 (22)	
Education				0.59			0.25			0.14
Nil or elementary	24 (28)	17 (25)	7 (37)		18 (24)	6 (46)		19 (24)	5 (56)	
Junior high school	32 (37)	26 (38)	6 (32)		29 (39)	3 (23)		30 (39)	2 (22)	
Senior high school or higher	31 (36)	25 (37)	6 (32)		27 (37)	4 (31)		29 (37)	2 (22)	
Smoking				0.21			0.360			0.08
Yes	76 (87)	61 (90)	15 (79)		66 (89)	10 (77)		70 (90)	6 (67)	
Alcohol				0.17			0.07			0.02
Yes	80 (92)	64 (94)	16 (84)		70 (95)	10 (77)		74 (95)	6 (67)	
Tumor location				0.49			0.09			0.44
Upper	13 (15)	9 (13)	4 (21)		10 (14)	3 (23)		11 (14)	2 (22)	
Middle	31 (36)	27 (40)	4 (21)		30 (41)	1 (8)		30 (39)	1 (11)	
Lower	20 (23)	15 (22)	5 (26)		16 (22)	4 (31)		17 (22)	3 (33)	
Overlapping	23 (26)	17 (25)	6 (32)		18 (24)	5 (39)		20 (26)	3 (33)	
Histological type				0.33			0.99			0.99
Squamous cell carcinoma	85 (98)	67 (99)	18 (95)		72 (97)	13 (100)		76 (97)	9 (100)	
Adenocarcinoma	2 (2)	1 (2)	1 (5)		2 (3)	0		2 (3)	0	
Stage				0.49			0.74			0.47
2	15 (17)	10 (15)	5 (26)		12 (16)	3 (23)		13 (17)	2 (22)	
3	61 (70)	49 (72)	12 (63)		52 (70)	9 (69)		54 (69)	7 (78)	
4	11 (13)	9 (13)	2 (11)		10 (14)	1 (8)		11 (14)	0	
Charlson Comorbidity Index				0.71			0.24			0.49
0	45 (52)	37 (54)	8 (42)		41 (55)	4 (31)		42 (54)	3 (33)	
1	16 (18)	12 (18)	4 (21)		13 (18)	3 (23)		14 (18)	2 (22)	
≥2	26 (30)	19 (28)	7 (37)		20 (27)	6 (46)		22 (28)	4 (44)	
ECOG performance				0.43			0.50			0.57
0	50 (58)	41 (60)	9 (47)		44 (60)	6 (46)		46 (59)	4 (44)	
1	35 (40)	26 (38)	9 (47)		28 (38)	7 (54)		30 (39)	5 (56)	
2	2 (2)	1 (2)	1 (5)		2 (3)	0		2 (3)	0	

ECOG: Eastern Cooperative Oncology Group, BMI: Body mass index

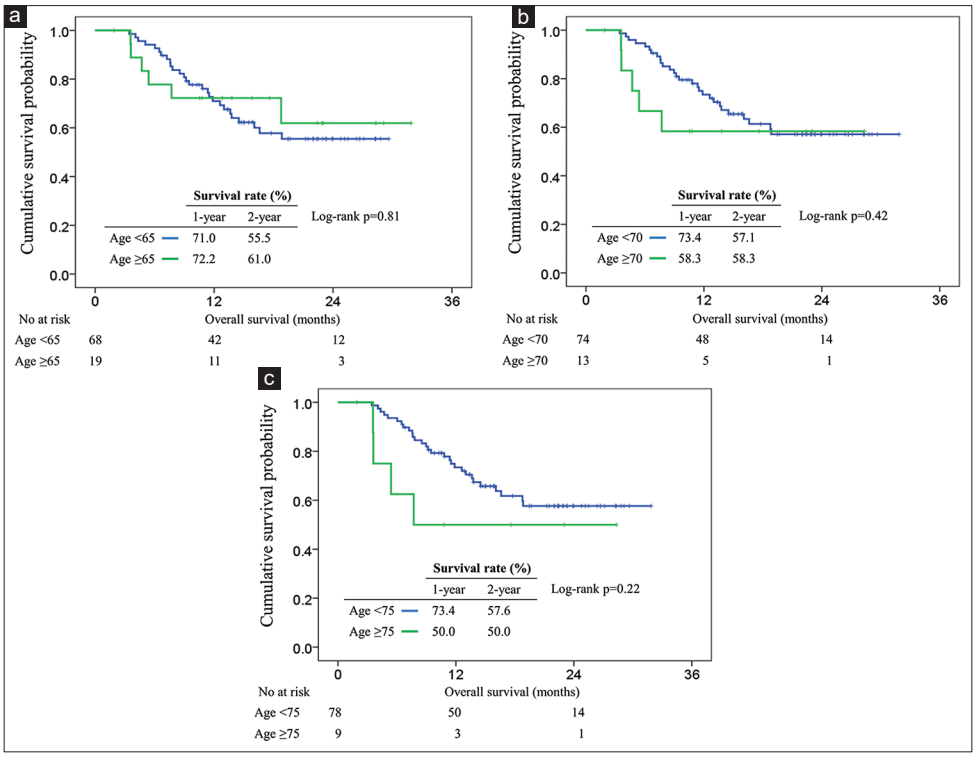


Figure 2: Survival outcomes stratify for patients aged <65 years versus ≥65 years (a), aged <70 years versus ≥70 years (b), and aged <75 years versus ≥75 years (c)

of patients receiving surgery was comparable between the patients aged <65 years and those aged ≥65 years (49% vs. 53%, $P = 0.80$). The percentages of patients receiving surgery were lower in the patients aged ≥70 and ≥75 years (53% and 31% for patients <70 years and ≥70 years, $P = 0.23$; 51% and 33% for patients <75 years and ≥75 years, $P = 0.48$); however, the differences between the younger and older patients did not reach significance.

Of the 43 patients who underwent surgical resection, 77% had complete resection with negative margins (R0 resection). Pathological response was further evaluated based on tumor regression grade: Grade 1 (no evidence of vital residual tumor cells) was observed in 18 patients (41.9%), Grade 2 (<10% residual tumor) in 7 patients (16.3%), Grade 3 (10%–50% residual tumor) in 12 patients (27.9%), and Grade 4 (>50% residual tumor) in 6 patients (14.0%). The resection rate and tumor regression grade were consistent across all age groups, with no significant differences observed [Supplementary Table 1].

Concurrent chemoradiotherapy-related complication

Analysis of CCRT-related complications across age subgroups revealed no significant differences [Table 3]. The incidence of incomplete chemotherapy in the overall cohort was 12%, with all occurrences observed in patients <65 years. The average percentage of planned chemotherapy dose actually administered was comparable among the age groups: patients aged <65 years received 88% (range 50%–100%) and those aged ≥65 years received 94% (range 80%–100%). Similar results were noted between the patients aged <70 years (89%, range 50%–100%) vs. ≥70 years (95%, range 80%–100%) and those aged <75 years (89%, range 50%–100%) vs. ≥75 years (96%, range 85%–100%). Although incomplete chemotherapy was slightly more frequent in the younger patients, overall chemotherapy dose completion remained high across all age subgroups. The incidence of incomplete radiotherapy in the overall cohort was 6%, with all occurrences observed in patients <65 years of age. There were no significant differences in incomplete radiotherapy across the age groups. The rates of ER visits and unplanned hospitalizations were 30% and 24%, respectively, with no significant differences among the age subgroups. However, ER visits were slightly more prevalent in the <65-year group, and unplanned hospitalizations were slightly more prevalent in the ≥65-year group. These findings suggested that CCRT-related complications were relatively consistent across the age subgroups, with no significant discrepancies observed.

Adverse events of concurrent chemoradiotherapy

Table 4 shows that sAEs (grade 3 or higher) were common during CCRT, with 75% of the overall cohort experiencing some form of toxicity. While the incidence of any toxicity was slightly higher in the patients ≥75 years compared to those <75 years, this difference did not reach significance ($P = 0.10$). Hematological toxicities, including leukopenia, anemia, neutropenia, and thrombocytopenia, were observed in 40% of the patients, and the prevalence of these toxicities did not differ significantly across age groups. Leukopenia was the most prevalent hematological toxicity, affecting 32% of the

Table 2: Efficacy of concurrent chemoradiotherapy by age subgroup

Efficacy	All (n=87), n (%)	Age <65 (n=68), n (%)	Age ≥65 (n=19), n (%)	P	Age <70 (n=74), n (%)	Age ≥70 (n=13), n (%)	P	Age <75 (n=78), n (%)	Age ≥75 (n=9), n (%)	P
Objective response rate	66 (76)	51 (75)	15 (79)	0.38	57 (77)	9 (69)	0.57	60 (77)	6 (67)	0.67
Surgical resection	43 (49)	33 (49)	10 (53)	0.80	39 (53)	4 (31)	0.23	40 (51)	3 (33)	0.48
R0 resection among 43 resected patients	33 (77)	26 (79)	7 (70)	0.67	29 (74)	4 (100)	0.56	30 (75)	3 (100)	0.99

Table 3: Concurrent chemoradiotherapy-related complications by age subgroup

Complications	All (n=87), n (%)	Age <65 (n=68), n (%)	Age ≥65 (n=19), n (%)	P	Age <70 (n=74), n (%)	Age ≥70 (n=13), n (%)	P	Age <75 (n=78), n (%)	Age ≥75 (n=9), n (%)	P
Incomplete chemotherapy	10 (12)	10 (15)	0	0.11	10 (14)	0	0.34	10 (13)	0	0.59
Average percentage of planned chemotherapy dose (range)	93% (50–100)	88% (50–100)	94% (80–100)	0.13	89% (50–100)	95% (80–100)	0.22	89% (50–100)	96% (85–100)	0.33
Incomplete radiotherapy	5 (6)	5 (7)	0	0.58	6 (7)	0	0.99	5 (6)	0	0.99
Emergency room visiting	26 (30)	21 (31)	5 (26)	0.78	22 (30)	4 (31)	0.99	22 (28)	4 (44)	0.44
Unplanned hospitalization	21 (24)	15 (22)	6 (32)	0.39	16 (22)	5 (39)	0.19	17 (22)	4 (44)	0.21

Table 4: Severe adverse events (≥ grade 3) by age subgroup

AE	All (*n*=87), *n* (%)	Age <65 (*n*=68), *n* (%)	Age ≥65 (*n*=19), *n* (%)	*P*	Age <70 (*n*=74), *n* (%)	Age ≥70 (*n*=13), *n* (%)	*P*	Age <75 (*n*=78), *n* (%)	Age ≥75 (*n*=9), *n* (%)	*P*
Any toxicity	65 (75)	50 (74)	15 (79)	0.77	53 (72)	12 (92)	0.17	56 (72)	9 (100)	0.10
Any hematological toxicity	35 (40)	27 (40)	8 (42)	0.99	28 (38)	7 (54)	0.28	30 (39)	5 (56)	0.48
Leukopenia	28 (32)	21 (31)	7 (37)	0.62	22 (30)	6 (46)	0.24	24 (31)	4 (44)	0.46
Anemia	15 (17)	11 (16)	4 (21)	0.73	11 (15)	4 (31)	0.23	12 (15)	3 (33)	0.18
Neutropenia	15 (17)	13 (19)	2 (11)	0.51	13 (18)	2 (15)	0.99	14 (18)	1 (11)	0.99
Thrombocytopenia	9 (10)	8 (12)	1 (5)	0.68	8 (11)	1 (8)	0.99	9 (12)	0	0.59
Neutropenic fever	4 (5)	4 (6)	0	0.57	4 (5)	0	0.99	4 (5)	0	0.99
Any nonhematological toxicity	45 (52)	35 (52)	10 (53)	0.93	38 (51)	7 (54)	0.87	40 (51)	5 (56)	0.99
Mucositis	20 (23)	16 (24)	4 (21)	0.82	17 (23)	3 (23)	0.99	17 (22)	3 (33)	0.42
Infection	15 (17)	13 (19)	2 (11)	0.51	13 (18)	2 (15)	0.99	13 (17)	2 (22)	0.65
Hyponatremia	8 (9)	6 (9)	2 (11)	0.99	6 (8)	2 (15)	0.34	6 (8)	2 (22)	0.19
Emesis	7 (8)	6 (9)	1 (5)	0.99	6 (8)	1 (8)	0.99	7 (9)	0	0.99
Hypertension	5 (6)	2 (3)	3 (16)	0.07	2 (3)	3 (23)	0.022	3 (4)	2 (22)	0.08
Hyperglycemia	5 (6)	4 (6)	1 (5)	0.99	5 (7)	0	0.99	5 (6)	0	0.99

AE: Adverse event

patients, followed by anemia (17%), neutropenia (17%), and thrombocytopenia (10%).

Non-hematological toxicities were reported in 52% of the cohort, with mucositis being the most common (23%), followed by infection (17%), hyponatremia (9%), and hypertension (6%). Notably, the rate of hypertension was significantly higher in the patients aged ≥70 years compared to those <70 years (23% vs. 3%, $P = 0.022$). However, there were no significant differences in other nonhematological toxicities across the age subgroups.

Discussion

The present study assessed the impact of age on the outcomes of CCRT in older patients with esophageal cancer. The findings suggest that age did not significantly influence survival outcomes, treatment efficacy, or the incidence of CCRT-related complications and adverse events, except for a higher prevalence of hypertension among the older patients. The comparable survival rates observed across age groups are consistent with previous studies that have demonstrated the feasibility and efficacy of CCRT in older patients with esophageal cancer.[21-23] This suggests that chronological age alone should not preclude the use of CCRT in this patient population, and a comprehensive assessment of functional status, comorbidities, and overall health should guide the treatment decision-making process.[18]

The similar efficacy of CCRT, as assessed by ORR, across age subgroups further supports that age is not a significant determinant of treatment outcomes. These findings are in line with studies on the management of other malignancies, which have shown the relative benefits of therapy in appropriately selected patients, even in those who are older.[24-26] However, it is important to note that the incidence of certain adverse events, particularly hypertension, was higher in the older patients. This underscores the importance of closely monitoring and managing comorbidities during CCRT in older patients.[17,27,28] The higher prevalence of hypertension in the older patients may be due to the cumulative effects of the chemotherapeutic agents and radiation therapy on the cardiovascular system,[18,29] as well as the increased susceptibility of older individuals to such toxicities. Given the potential for adverse effects, it is crucial to closely monitor and actively manage any comorbidities in older patients during the course of CCRT to optimize their care and treatment outcomes.[30,31]

In addition to chronological age, physiological reserve plays a critical role in treatment tolerance and outcomes in esophageal cancer patients. Frailty, characterized by reduced nutritional status, comorbidity burden, and diminished physical or social support, can predispose patients to severe treatment-related toxicity. In our previous prospective study involving the same patient population, frailty was found to be independently associated with higher risks of hematologic toxicity, ER visits, and hospitalization, as well as worse overall and disease-free survival during and after CCRT.[32] These findings emphasize

that pretreatment frailty assessment should be considered an essential component of clinical decision-making, particularly for older adults or those with functional decline due to dysphagia or malnutrition. The findings of this study are further supported by previous studies, which have also shown that when appropriate patient selection and comprehensive geriatric assessments are employed, older patients can derive similar benefits from cancer therapies as their younger counterparts, including surgery, chemotherapy, and radiation.[18,25] The cooperation between geriatric and oncology specialists is essential in developing predictive models and improving decision-making for older cancer patients.[33]

This study is strengthened by its real-world nature, which enhances the generalizability of the findings to the broader population of older patients with esophageal cancer. However, several limitations inherent to the retrospective design must be acknowledged. First, there is a risk of selection bias. Patients included in this study were deemed eligible for CCRT by their treating physicians, likely based on preserved functional status, manageable comorbidities, and willingness to undergo intensive therapy. As such, older patients with significant frailty, advanced comorbidities, or poor performance status may not have been offered CCRT and were therefore excluded. This may have led to a healthier older cohort, limiting generalizability to the broader population of older adults with esophageal cancer. In addition, retrospective data collection may be subject to incomplete documentation and missing variables that could influence outcomes. Treatment decisions were not standardized across the three institutions, introducing potential heterogeneity. Another limitation is the relatively small sample size, which may have limited the statistical power to detect more subtle differences in outcomes across age groups. The median follow-up duration was 21.5 months, which limited the ability to report long-term survival metrics such as 3-year or 5-year OS. Finally, only 10% of the patients were aged ≥75 years, and the results may not be fully representative of very old patients with esophageal cancer. In addition, we did not perform multivariate analysis to adjust for potential confounding variables such as performance status, comorbidity burden, or tumor stage. While univariate analysis did not show significant survival differences across age groups and the baseline characteristics were generally balanced, the absence of multivariate modeling limits our ability to determine the independent prognostic impact of age. Despite these limitations, the real-world nature of this study still offers valuable insights into the tolerability and efficacy of CCRT in a carefully selected older population. Further studies are warranted to confirm the findings in larger, more diverse cohorts of older patients.

Conclusion

This study evaluated the impact of age on the outcomes of CCRT in older patients with esophageal cancer. The results suggest that chronological age alone should not be a contraindication to CCRT in esophageal cancer patients with adequate performance status and organ function**.** However, these findings apply to a carefully selected older population, and caution should be exercised when generalizing to more frail or comorbid older adults.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Conflicts of interest

Dr. Wen-Chi Chou, the Deputy Editor-in-Chief at *Journal of Cancer Research and Practice*, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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Supplementary Table 1: Tumor regression grade and resection status according to different age groups

Variables	All (n=43), n (%)	Age <65 (n=33), n (%)	Age ≥65 (n=10), n (%)	P	Age <70 (n=39), n (%)	Age ≥70 (n=4), n (%)	P	Age <75 (n=40), n (%)	Age ≥75 (n=3), n (%)	P
Resection status				0.56			0.59			0.44
R0	33 (76.7)	26 (78.8)	7 (70)		29 (74.4)	4 (100)		30 (75)	3 (100)	
R1	8 (18.6)	5 (15.2)	3 (30)		8 (20.5)	0		8 (20)	0	
R2	2 (4.7)	2 (6.0)	0		2 (5.1)	0		2 (5)	0	
Tumor regression grade				0.39			0.16			0.69
1 (pathological complete response)	18 (41.9)	14 (42.4)	4 (40)		17 (46.3)	1 (25)		17 (42.5)	1 (33.3)	
2 (<10% residual tumor)	7 (16.3)	6 (18.2)	1 (10)		7 (17.9)	0		7 (17.5)		
3 (10%–50% residual tumor)	12 (27.9)	10 (30.3)	2 (10)		11 (28.2)	1 (25)		11 (27.5)	1 (33.3)	
4 (>50% residual tumor)	6 (14.0)	3 (9.1)	3 (30)		4 (10.3)	2 (50)		5 (12.5)	1 (33.3)	