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Research

Impact of preoperative comorbidities on elderly patients with esophageal squamous cell carcinoma following esophagectomy: a propensity score matching analysis

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Abstract

Objective Elderly patients, particularly those aged 70 and above, often present with comorbidities such as coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), and high blood pressure (HBP). These comorbid diseases complicate treatment. However, the impact of these comorbidities on survival outcomes and complications in elderly patients undergoing esophagectomy for esophageal squamous cell carcinoma (ESCC) remains under-researched.

Methods This cohort study examined ESCC patients aged 70 and older who underwent esophagectomy. Patients were divided into two cohorts: those without preoperative comorbid diseases (NCD group) and those with preoperative comorbid diseases (CD group). Data were obtained from the Sichuan Cancer Hospital and Institute Esophageal Cancer Case Management Database between May 2016 and August 2021, with follow-up concluding on December 20, 2023.

Results A total of 469 patients met the inclusion criteria, with 206 patients in the comorbid diseases (CD group) and 263 patients without (NCD group). The median follow-up period was 47.5 months, the median overall survival (OS) was 51.6 months and median disease-free survival (DFS) was 33.0 months, with no statistically significant difference in OS and DFS in 2 groups. The incidence of grade 3 or higher complications in the NCD and CD groups was similar, with no statistically significant difference. The most common grade 3 or higher complications were pulmonary infection, hydrothorax, anastomotic stenosis, and anastomotic leakage.

Conclusions Preoperative comorbidities, including CHD, COPD, DM, and HBP, did not significantly impact the long-term survival or disease-free survival of elderly ESCC patients undergoing esophagectomy.

Abbreviations

ESCC	Esophageal squamous cell carcinoma
EC	Esophageal cancer
OS	Overall surviva
DFS	Disease-Free Survival

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RMST	Restricted mean survival time
RMDFST	Restricted Mean Disease-Free Survival Time
HRs	Hazard ratios
CIs	Confidence intervals
BMI	Body mass index
WHO	World Health Organization
PSM	Performing propensity score matching
KPS	Karnofsky Performance Status
IPTW	Inverse probability of treatment weighting
OW	Overlap weighting
CHD	Coronary heart disease
COPD	Chronic obstructive pulmonary disease
HBP	High blood pressure
DM	Diabetes mellitus
UICC/AJCC	Union for International Cancer Control/American Joint Committee on Cancer
SCCH-ECCM Database	Sichuan Cancer Hospital & Institute Esophageal Cancer Case Management Database

1 Introduction

Esophageal cancer (EC) poses a significant global health challenge, ranking as the sixth leading cause of cancer-related deaths worldwide, with over 500,000 new cases diagnosed annually [1,2]. Surgical resection remains the cornerstone of comprehensive treatment for esophageal cancer, frequently combined with neoadjuvant chemotherapy, chemoradiotherapy, or immunotherapy [3–7]. Postoperative management strategies, including adjuvant chemotherapy, radiation therapy, or immunotherapy, are implemented based on the patient's condition [3,8,9]. The survival of patients with esophageal cancer is influenced by numerous factors, including lifestyle choices such as smoking and alcohol consumption, which not only affect the tumor's response to treatment but also significantly impact patient prognosis [10–14].

In recent years, the survival rates of esophageal cancer patients have improved due to advancements in therapeutic approaches. In the 2023 study, the global five-year survival rate for esophageal cancer is approximately 21% [1,2]. However, this figure remains low, primarily due to the advanced stage of the disease at diagnosis for many patients. Furthermore, the aging population significantly contributes to this issue, with older adults representing a growing proportion of esophageal cancer cases [1,15,16]. Elderly patients, particularly those over 70 years old, often contend with comorbidities such as coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), and high blood pressure (HBP), which complicate their treatment and management [17].

According to the Global Burden of Disease 2019 Study, the primary causes of death among individuals aged 70 and older include ischemic heart disease, stroke, COPD, Alzheimer's disease, and lower respiratory infections [17]. These comorbidities not only diminish the efficacy of treatment in patients with esophageal squamous cell carcinoma (ESCC) but also complicate postoperative care and contribute to elevated mortality rates [18–20]. Despite the increasing prevalence of comorbidities in older patients, the influence of these conditions on survival and postoperative complications in individuals undergoing esophagectomy for ESCC remains inadequately studied.

In this study, we aimed to investigate the survival outcomes and postoperative complications of ESCC patients aged 70 and above who underwent esophagectomy. Specifically, we compared outcomes between two cohorts: patients without preoperative comorbidities and those with preoperative comorbidities, including CHD, COPD, DM, and HBP. By employing Kaplan–Meier survival analysis and restricted mean survival time (RMST) estimates, we sought to determine whether the presence of these comorbidities affects long-term survival and the risk of complications following surgery.

2 Methods

2.1 Study design

This retrospective cohort study was conducted using data from the Sichuan Cancer Hospital & Institute Esophageal Cancer Case Management Database (SCCH-ECCM Database). The study focused on patients aged 70 and above who were diagnosed with esophageal squamous cell carcinoma (ESCC) and underwent esophagectomy between May 2016 and August 2021. Patients were included if they met specific criteria: thoracic esophageal carcinoma, squamous cell carcinoma pathology and no distant metastasis. Exclusion criteria included tumors located outside the thoracic region, non-squamous cell carcinoma pathology and missing data (Fig. 1). The final follow-up date was December 20, 2023. The research is being reported in line with the STROBE guidelines [21].

3 Grouping and Outcome Measures

Patients were categorized into two groups based on the presence of comorbidities: those without preoperative comorbid diseases (NCD group) and those with preoperative comorbid diseases (CD group), which included CHD, COPD, DM, and HBP. The clinical data collected encompassed demographic information, tumor characteristics, and postoperative outcomes. Disease staging was conducted in accordance with the 8th edition TNM classification established by the UICC/AJCC criteria [22]. Pathological findings were reviewed by two pathologists and validated for accuracy by a third expert.

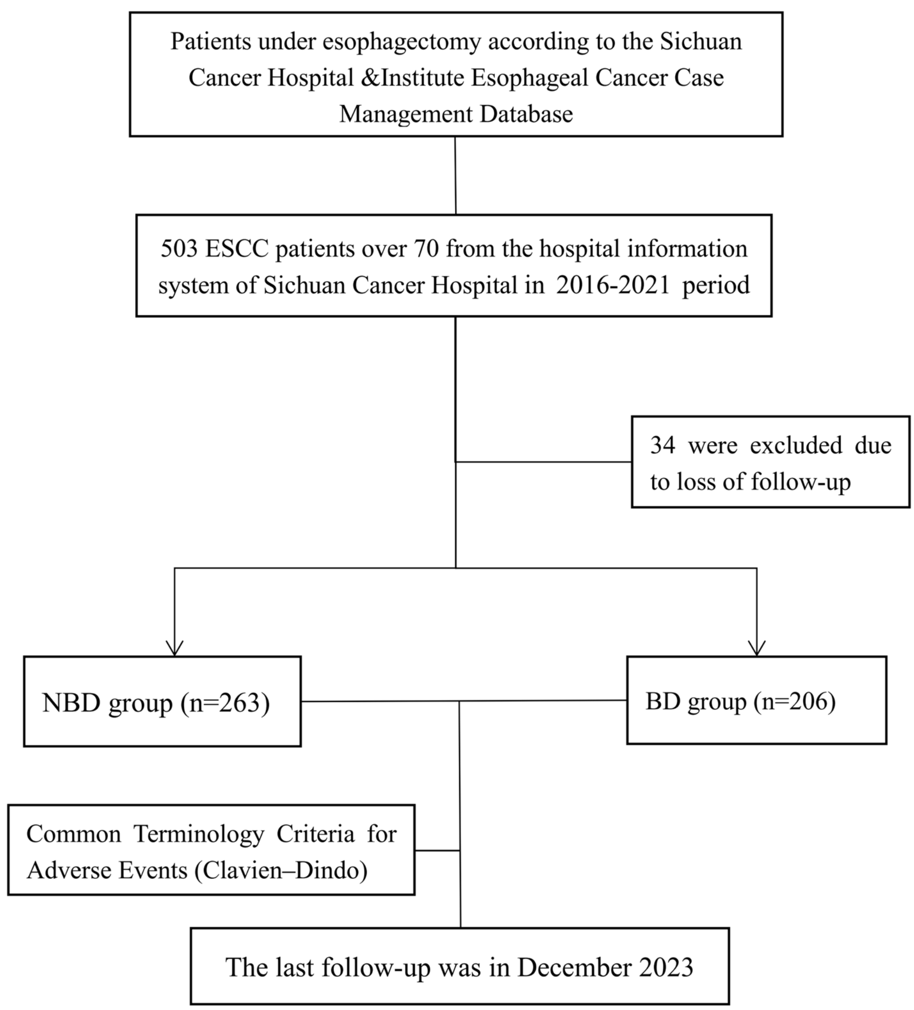


Fig. 1 CONSORT diagram of patient selection. *NCD* Non-Comorbid Disease, *CD* Comorbid Disease

We categorized comorbidities using a grading system, where the majority of complications observed were classified as Grade I. These Grade I complications primarily included manageable conditions that could be effectively treated with medication.

4 Criteria and characteristics of the adverse events

To account for variations in patients' body compositions, body mass index (BMI) was categorized into three levels according to international standards established by the World Health Organization (WHO) [23,24]. Furthermore, surgical complications were classified utilizing the Clavien-Dindo classification system, as endorsed by the International Consensus on Standardization of Data Collection for Complications Associated with Esophagectomy [25–27].

5 Statistical analysis

Descriptive statistics are presented as means and standard deviations for continuous variables, and counts and percentages for categorical variables. Kaplan–Meier survival curves were generated for overall survival (OS) and Disease-Free Survival (DFS). Comparisons between groups were made using the log-rank test. RMST and Restricted Mean Disease-Free Survival Time (RMDFST) estimates along with 95% confidence intervals (CIs) were calculated for both groups based on Kaplan–Meier estimates. Hazard ratios (HRs) and 95% CIs were determined using Cox proportional hazards regression models to identify independent risk factors for OS. Univariate Cox regression analyses were performed, followed by multivariate analysis to adjust for potential confounders including age, sex, tumor stage, and presence of comorbidities. Propensity score matching (PSM) was employed to balance covariates between the no comorbidity and comorbidity groups and ensure a fair comparison of survival outcomes. Nearest neighbor matching without replacement was performed based on propensity scores derived from a logistic regression model including relevant covariates. Sensitivity analyses using inverse probability of treatment weighting (IPTW) and overlap weighting (OW) methods were also conducted to validate the results. All statistical analyses were performed using RStudio software running R version 4.3.0. A significance level of $p < 0.05$ was set for all analyses.

Ethical Considerations.

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee for Medical Research and New Medical Technology of Sichuan Cancer Hospital (SCCHEC-02–2024-191). The need for informed consent was waived by Ethics Committee for Medical Research and New Medical Technology of Sichuan Cancer Hospital (SCCHEC-02–2024-191).

6 Results

6.1 Patient characteristics

A total of 469 patients aged 70 and above who underwent esophagectomy were included in this study. Among them, 27 patients were aged 80 or older (5.8%), while the remaining 442 patients were between 70 and 79 years old (94.2%). The cohort comprised 375 males (80.0%) and 94 females (20.0%). More than half of the patients reported a history of smoking and alcohol consumption. In terms of preoperative status, 350 patients (74.6%) had a Karnofsky Performance Status (KPS) score of 90–100, indicating a relatively good condition, whereas 119 patients (25.4%) had a KPS score below 90. Regarding BMI, 34 patients (7.2%) were categorized as Low-BMI, 360 patients (76.8%) as Normal-BMI, and 75 patients (16.0%) as High-BMI. A total of 206 patients had comorbid diseases (CD group), including CHD in 14 patients, COPD in 55 patients, DM in 47 patients, and HBP in 144 patients. The remaining 263 patients did not have any of these 4 chronic comorbid diseases. Preoperative clinical TNM (cTNM) staging identified 342 patients (72.9%) as stage III or IVA, with 72 patients receiving neoadjuvant therapy. Postoperative pathological TNM (pTNM) staging revealed that 227 patients (48.4%) were classified as stage III or IVA (Table 1 and Table 2).

Table 1 Demographic characteristics of the 2 groups

Characteristic	Before PSM		*P* value	After PSM		*P* value
	NCD Group	CD Group		NCD Group	CD Group	
Gender			0.528			0.780
Male	213 (80.99)	162 (78.64)		128 (80.50)	126 (79.25)	
Female	50 (19.01)	44 (21.36)		31 (19.50)	33 (20.75)	
Age, years			0.955			0.608
< 80	248 (94.3)	194 (94.17)		152 (95.60)	150 (94.34)	
≥ 80	15 (5.70)	12 (5.83)		7 (4.40)	9 (5.66)	
KPS			< 0.001			0.058
< 90	214 (81.37)	136 (66.02)		131 (82.39)	117 (73.58)	
≥ 90	49 (18.63)	70 (33.98)		28 (17.61)	42 (26.42)	
BMI			0.065			0.961
Low-BMI	21 (7.98)	13 (6.31)		12 (7.55)	13 (8.18)	
Normal-BMI	209 (79.47)	151 (73.30)		126 (79.25)	124 (77.99)	
High-BMI	33 (12.55)	42 (20.39)		21 (13.21)	22 (13.84)	
Smoker			0.874			0.575
No	127 (48.29)	101 (49.03)		74 (46.54)	79 (49.69)	
Yes	136 (51.71)	105 (50.97)		85 (53.46)	80 (50.31)	
Drinker			0.478			0.501
No	120 (45.63)	103 (50.00)		73 (45.91)	79 (49.69)	
Yes	143 (54.37)	103 (50.00)		86 (54.09)	80 (50.31)	
Tumor location			0.172			0.923
Upper	31 (11.79)	30 (14.56)		21 (13.21)	23 (14.47)	
Middle	126 (47.91)	81 (39.32)		63 (39.62)	64 (40.25)	
Lower	106 (40.3)	95 (46.12)		75 (47.17)	72 (45.28)	
cT category			0.634			0.819
T1	17 (6.46)	12 (5.83)		7 (4.40)	9 (5.66)	
T2	34 (12.93)	33 (16.02)		20 (12.58)	24 (15.09)	
T3	187 (71.10)	137 (66.50)		114 (71.70)	111 (69.81)	
T4	25 (9.51)	24 (11.65)		18 (11.32)	15 (9.43)	
cN category			0.602			0.974
N0	44 (16.73)	37 (17.96)		29 (18.24)	30 (18.87)	
N1	164 (62.36)	118 (57.28)		96 (60.38)	98 (61.64)	
N2	51 (19.39)	49 (23.79)		33 (20.75)	30 (18.87)	
N3	4 (1.52)	2 (0.97)		1 (0.63)	1 (0.63)	
cTNM stage			0.999			0.914
I	15 (5.70)	12 (5.83)		7 (4.40)	9 (5.66)	
II	56 (21.29)	44 (21.36)		35 (22.01)	36 (22.64)	
III	161 (61.22)	125 (60.68)		98 (61.64)	98 (61.64)	
IV	31 (11.79)	25 (12.14)		19 (11.95)	16 (10.06)	
Pathologic differentiation grade			0.828			0.899
Well G1-Moderate G2	78 (29.66)	63 (30.58)		42 (26.42)	43 (27.04)	
Poor or undifferentiated G3	185 (70.34)	143 (69.42)		117 (73.58)	116 (72.96)	
Neoadjuvant.therapy			0.540			0.877
No	225 (85.55)	172 (83.50)		134 (84.28)	135 (84.91)	
Yes	38 (14.45)	34 (16.50)		25 (15.72)	24 (15.09)	

KPS Karnofsky Performance Status, *PSM* propensity score matching, *TNM* tumor, node, metastasis, *CRT* chemoradiotherapy, *CT* chemotherapy, *MIE* minimally invasive esophagectomy, *OE* open esophagectomy, *RT* radiotherapy

Table 2 Details after esophagectomy in 2 groups

Characteristic	Before PSM		*P* value	After PSM		*P* value
	NCD Group	CD Group		NCD Group	CD Group	
pT category			0.850			0.558
T0	8 (3.04)	4 (1.94)		7 (4.40)	2 (1.26)	
T1	38 (14.45)	35 (16.99)		22 (13.84)	26 (16.35)	
T2	55 (20.91)	39 (18.93)		28 (17.61)	29 (18.24)	
T3	151 (57.41)	118 (57.28)		94 (59.12)	94 (59.12)	
T4	11 (4.18)	10 (4.85)		8 (5.03)	8 (5.03)	
pN category			0.717			0.662
N0	131 (49.81)	113 (54.85)		81 (50.94)	88 (55.35)	
N1	80 (30.42)	55 (26.70)		55.35 (46.50)	44 (46.50)	
N2	40 (15.21)	28 (13.59)		23 (14.47)	18 (11.32)	
N3	12 (4.56)	10 (4.85)		6 (3.77)	9 (5.66)	
p8th TNM stage			0.772			0.565
I	48 (18.25)	40 (19.42)		30 (18.87)	30 (18.87)	
II	85 (32.32)	69 (33.50)		52 (32.70)	54 (33.96)	
III	113 (42.97)	80 (38.83)		68 (42.77)	60. (37.74)	
IV	17 (6.46)	17 (8.25)		9 (5.66)	15 (9.43)	
Lymphovascular invasion			0.120			0.481
No	179 (68.06)	126 (61.17)		106 (66.67)	100 (62.89)	
Yes	84 (31.94)	80 (38.83)		53 (33.33)	59 (37.11)	
Nerve invasion			0.23			0.216
No	155 (58.94)	110 (53.40)		91 (57.23)	80 (50.31)	
Yes	108 (41.06)	96 (46.60)		68 (42.77)	79 (49.69)	
Surgical approach			0.063			0.745
McKeown	235 (89.35)	172 (83.50)		136 (85.53)	138 (86.79)	
Iovr-Lewish	28 (10.65)	34 (16.50)		23 (14.47)	21 (13.21)	
Thoracic surgical type			0.172			0.793
MIE	207 (78.71)	151 (73.30)		122 (76.73)	120 (75.47)	
OE	56 (21.29)	55 (26.70)		37 (23.27)	39 (24.53)	
Complete resection			0.306			0.999
R0	252 (95.82)	200 (97.09)		156 (98.11)	155 (97.48)	
R1	11 (4.18)	5 (2.43)		3 (1.89)	3 (1.89)	
R2	0 (0.00)	1 (0.49)		0 (0)	1 (0.63)	
Circumferential resection margin			0.824			0.627
Negative	244 (92.78)	190 (92.23)		151 (94.97)	149 (93.71)	
Positive	19 (7.22)	16 (7.77)		8 (5.03)	10 (6.29)	
Clavien–Dindo			0.114			0.259
1–2	122 (46.39)	111 (53.88)		83 (52.20)	93 (58.49)	
3–5	141 (53.61)	95 (46.12)		76 (47.80)	66 (41.51)	
Died in 30 days	2 (1.55)	1 (0.90)	0.999	2 (2.74)	0 (0.00)	0.453
Died in 30–90 days	9 (6.98)	2 (1.80)	0.056	4 (5.48)	2 (2.60)	0.629
Died in 3–6 months	7 (5.43)	6 (5.41)	0.994	4 (5.48)	4 (5.19)	0.999

7 Overall Survival and Disease Free Survival

Among the 469 patients, the median follow-up period was 47.5 months. The median OS time was 51.6 months (95% CI: 38.10–65.10). There was no statistically significant difference in OS between the CD group and the NCD group. The median survival time for the CD group was 36.0 months (95% CI: 26.57–45.43), while it was 44.9 months (95% CI: 33.55–56.24) for the NCD group. The 1-, 3-, and 5-year OS rates for the CD group were 86%, 50%, and 42%, respectively,

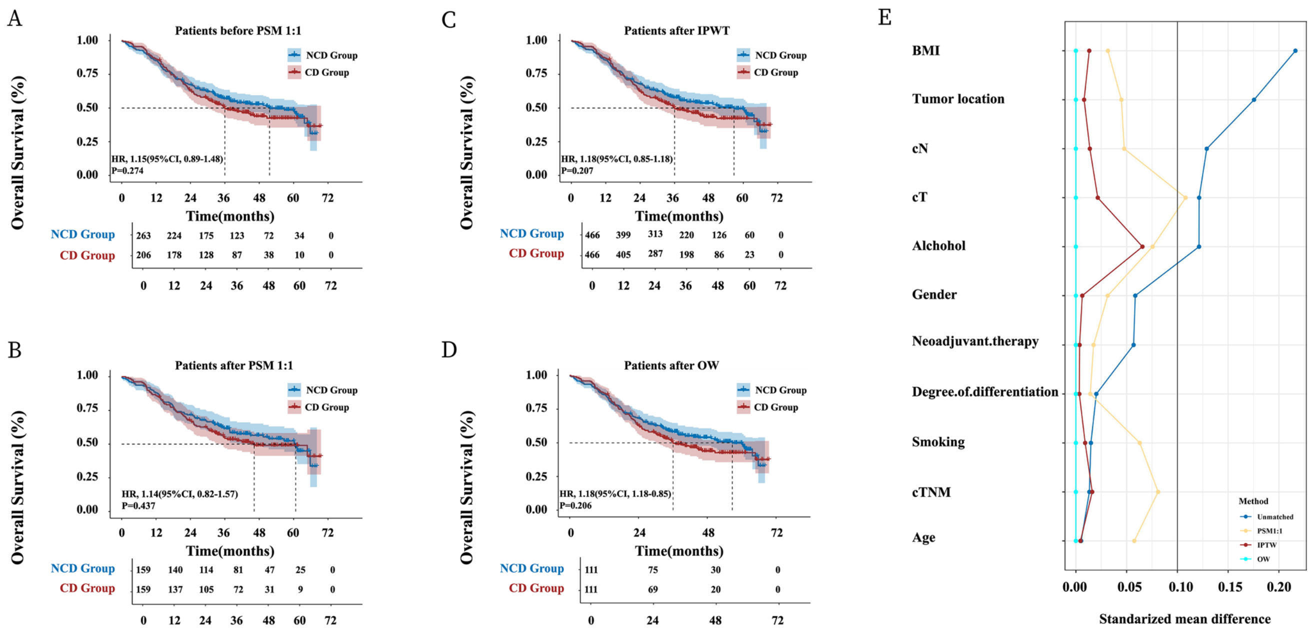


Fig. 2 Overall survival curves of participants in NCD and CD groups. **A** Overall survival curve of NCD and CD groups before PSM; **B** Overall survival curve of NCD and CD groups after PSM; **C** Overall survival curve of NCD and CD groups after IPTW; **D** Overall survival curve of NCD and CD groups after OW; **E** Standardized in the subjects stratified by characteristic

compared to 85%, 57%, and 48% for the NCD group. The unadjusted survival analysis showed a HR of 0.868 (95% CI: 0.67–1.12; P = 0.274), indicating no significant survival benefit between the two groups (Fig. 2A). After performing a 1:1 PSM analysis, there remained no statistically significant difference between the two groups, with an HR of 1.14 (95% CI: 0.82–1.57; P = 0.437; Fig. 2B). Similarly, after adjusting for IPTW, there was still no significant difference, with an HR of 1.18 (95% CI: 0.85–1.18; P = 0.207; Fig. 2C). The OW analysis also yielded no statistically significant difference, with an HR of 1.18 (95% CI: 0.85–1.18; P = 0.206; Fig. 2D).

The median DFS time was 33.0 months (95% CI: 38.10–65.10). There was no statistically significant difference in DFS between the CD group and the NCD group. The median DFS time for the CD group was 27.4 months (95% CI: 19.32–35.42), while it was 36.5 months (95% CI: 26.93–46.13) for the NCD group. The 1-, 3-, and 5-year DFS rates for the CD group were 75%, 45%, and 36%, respectively, compared to 74%, 51%, and 36% for the NCD group. The unadjusted survival analysis showed an HR of 0.968 (95% CI: 0.81–1.31; P = 0.791), indicating no significant DFS benefit between the two groups (Fig. 3A). After 1:1 PSM analysis, there was still no statistically significant difference between the two groups, with an HR of 0.98 (95% CI: 0.73–1.32; P = 0.908; Fig. 3B). The IPTW-adjusted analysis also showed no significant difference, with an HR of 1.03 (95% CI: 0.97–1.03; P = 0.805; Fig. 3C). The OW analysis yielded similar results, with an HR of 1.03 (95% CI: 0.97–1.03; P = 0.790; Fig. 3D). Figure 3E illustrated that for 1:1 PSM, IPTW, and OW methods, the SMD for all variables is less than 0.10.

8 Restricted Mean Survival Time and Restricted Mean Disease-Free Survival Time

Through further RMST analysis, the RMST for patients in the NCD group was 43.30 months (95% CI: 40.18–46.43). In the CD group, patients with HBP, DM, and COPD had an RMST of 47.94 months (95% CI: 31.48–64.41), which represented the highest value on the curve. The other subgroups with an RMST of over 40 months included patients with HBP, patients with COPD, and patients with both HBP and DM. Conversely, the subgroup of patients with HBP, DM, and CHD had the lowest RMST of 20.51 months (95% CI: 19.28–21.74), which marked the lowest point on the curve (Fig. 4A). The adjusted RMST results presented a similar trend. The RMST for patients in the NCD group was 41.14 months (95% CI: 37.66–44.61). In the CD group, patients with HBP had the highest RMST of 42.64 months (95% CI: 40.04–45.25). This was followed by patients with CHD, COPD, and those with both HBP and DM, with each subgroup having an RMST of over 40 months. On the other hand, patients with HBP, DM, and CHD had an RMST of 18.53 months (95% CI: 18.03–19.03), the lowest point on the curve. Other subgroups with the lowest RMST were patients with both DM and COPD, whose RMST was 23.52 months (95% CI: 22.74–24.29) (Fig. 4B).

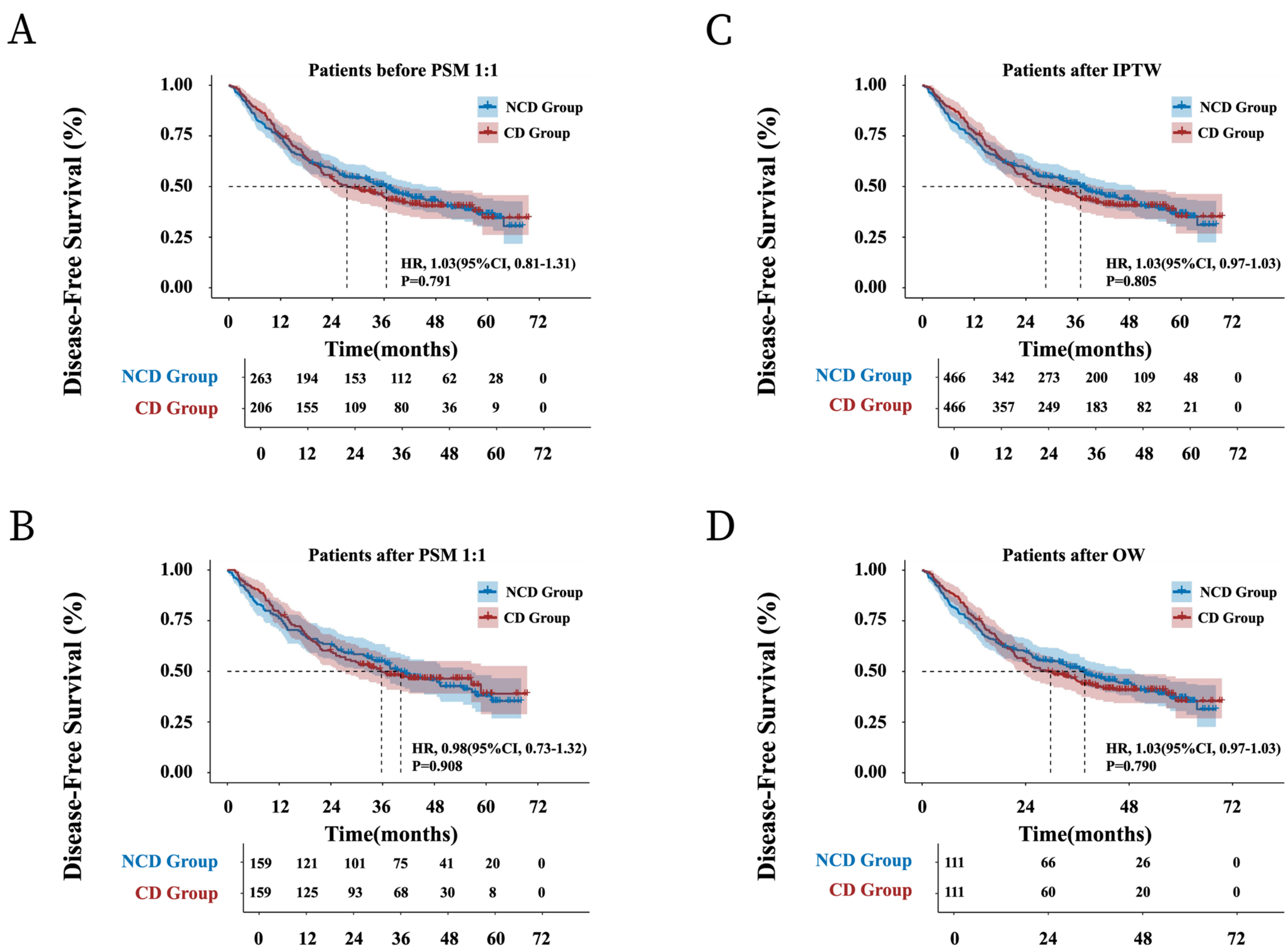


Fig. 3 Disease-free survival curves of participants in NCD and CD groups. **A** Disease-free survival curve of NCD and CD groups before PSM; **B** Disease-free survival curve of NCD and CD groups after PSM; **C** Disease-free survival curve of NCD and CD groups after IPTW; **D** Disease-free survival curve of NCD and CD groups after OW

In the RMDFS results, the NCD group had an RMDFS of 37.40 months (95% CI: 34.14–40.66). In the CD group, patients with HBP, DM, and COPD had an RMDFS of 47.94 months (95% CI: 31.48–64.41), representing the highest value on the curve. This was followed by the subgroup of patients with both HBP and DM, whose RMDFS also exceeded 40 months, at 40.84 months (95% CI: 29.54–52.14). Conversely, patients with HBP, CHD, and COPD had an RMDFS of 8.47 months (95% CI: 8.47–8.47), marking the lowest point on the curve (Fig. 4C). In the adjusted RMDFS results, the NCD group had an RMDFS of 36.91 months (95% CI: 33.24–40.57). In the CD group, patients with HBP had the highest RMDFS of 37.57 months (95% CI: 34.83–40.30), followed by patients with both HBP and DM, whose RMDFS was 35.96 months (95% CI: 33.61–38.32). At the other end of the spectrum, patients with HBP, CHD, and COPD had the lowest RMDFS of 7.73 months (95% CI: 7.58–7.90). Other subgroups with similarly low RMDFS values included patients with both DM and COPD (RMDFS of 17.01 months; 95% CI: 16.38–17.64) and patients with HBP, DM, and CHD (RMDFS of 16.77 months; 95% CI: 16.15–17.39) (Fig. 4D).

9 Short-term Outcomes and Adverse Events (Clavien-Dindo, 2009)

In the 469 patients included in the study, 233 (49.68%) experienced postoperative complications classified as grade 0–2 according to the Clavien-Dindo system, while 236 (50.32%) had complications classified as grade 3 or higher. Mortality within 30 days was 3 patients (0.64%), with 11 deaths (2.35%) occurring between 30 and 90 days, and 13 deaths (2.77%) within 90 days to six months postoperatively. In the NCD group, 122 patients (46.39%) had postoperative complications of Clavien-Dindo grade 0–2, while 141 patients (53.61%) experienced complications

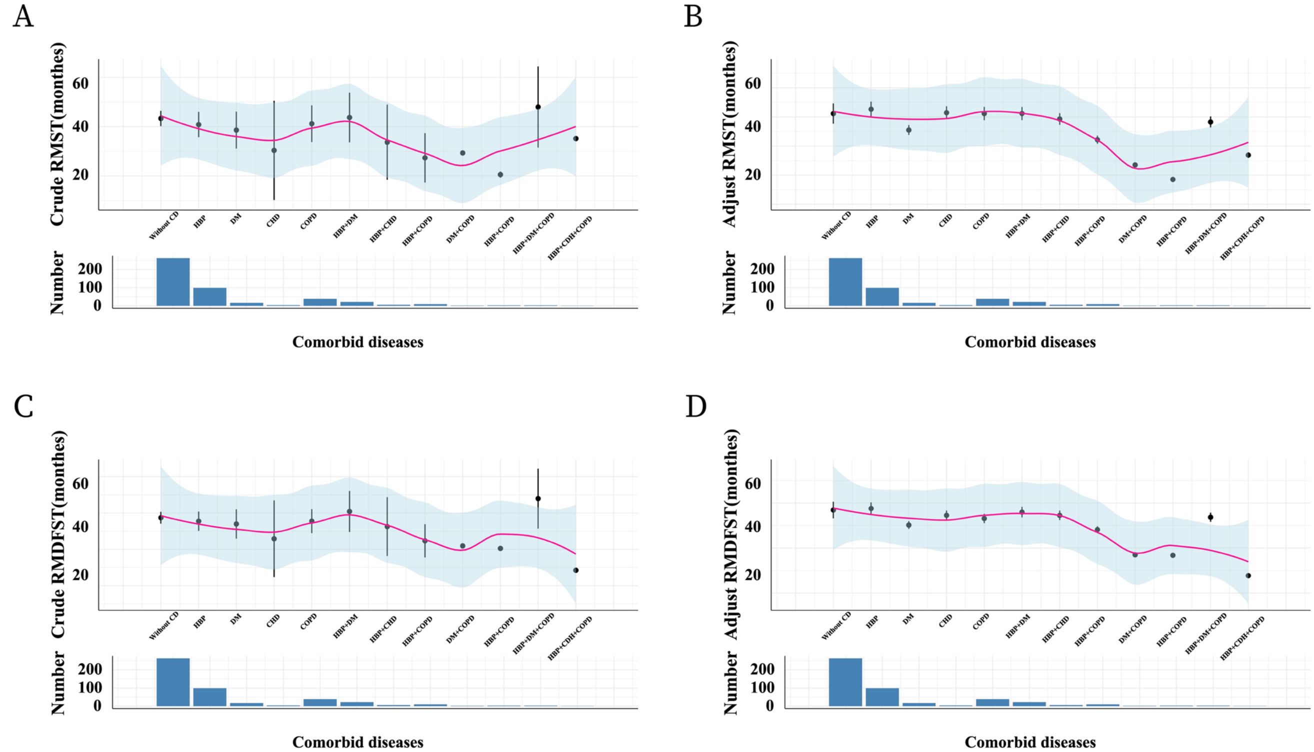


Fig. 4 Restricted mean survival time (RMST) and Restricted Mean Disease-Free Survival Time (RMDFST) estimates patients. **A** Crude RMST estimates different patients; **B** Adjust RMST estimates different patients; **C** Crude RMDFST estimates different patients; **D** Adjust RMDFST estimates different patients

of grade 3 or higher. In the CD group, 111 patients (53.88%) had complications classified as grade 0–2, and 95 patients (46.12%) had grade 3 or higher complications. There was no statistically significant difference between the two groups (P = 0.114), and after PSM, the difference remained non-significant (P = 0.259) (Table 2 and Table 3).

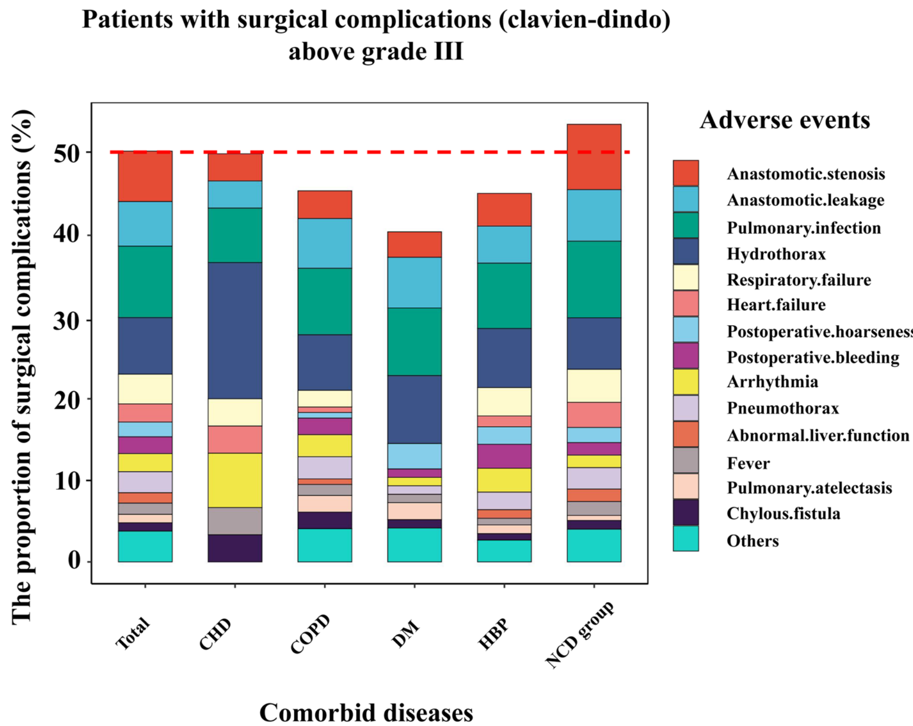
Among the total population, the incidence of grade 3 or higher complications (Clavien-Dindo) was 50.32%, with the most common being pulmonary infection (102 patients), hydrothorax (81 patients), anastomotic stenosis (72 patients), and anastomotic leakage (64 patients). In the NCD group, the incidence of grade 3 or higher complications was 53.61%, primarily including pulmonary infection (61 patients), hydrothorax (41 patients), anastomotic stenosis (52 patients), and anastomotic leakage (41 patients). In patients with preoperative HBP, the incidence of grade 3 or higher complications was 45.14%, with the most common issues being pulmonary infection (30 patients), hydrothorax (27 patients), anastomotic stenosis (15 patients), and anastomotic leakage (17 patients). In patients with preoperative DM, the incidence of grade 3 or higher complications was 40.43%, with pulmonary infection (8 patients), hydrothorax (8 patients), anastomotic stenosis (3 patients), and anastomotic leakage (6 patients) being most prevalent. Among patients with preoperative CHD, the incidence of grade 3 or higher complications was 50.00%, primarily including hydrothorax (5 patients), pulmonary infection (2 patients), and arrhythmia (2 patients). In patients with preoperative COPD, the incidence of grade 3 or higher complications was 45.45%, with the most frequent complications being pulmonary infection (12 patients), hydrothorax (10 patients), anastomotic leakage (9 patients), and anastomotic stenosis (5 patients) (Fig. 5 and Table 3).

In terms of Clavien-Dindo grade 3 complications, the NCD group had a higher incidence of anastomotic stenosis (P = 0.004), and this difference remained significant after PSM (P = 0.007). Conversely, the CD group exhibited a higher incidence of arrhythmia (P = 0.019). For Clavien-Dindo grade 4 complications, the incidence rates of various complications were comparable between the two groups. Among Clavien-Dindo grade 3–5 complications, the NCD group experienced higher rates of anastomotic stenosis (P = 0.003) and heart failure (P = 0.028). After PSM, the NCD group continued to show a higher incidence of anastomotic stenosis (P = 0.007), while the CD group had higher rates of postoperative bleeding (P = 0.047) and arrhythmia (P = 0.029) (Table 3 and Fig. 6).

Table 3 Postoperative complications (Clavien–Dindo) of grade 3 or above in patients

Adverse events	Before PSM						After PSM					
	NCD Group (n = 263)			CD Group (n = 206)			NCD Group (n = 159)			CD Group (n = 159)		
	III	IV	V	III	IV	V	III	IV	V	III	IV	V
Anastomotic stenosis	51 (19.39)	1 (0.38)		20 (9.71)			32 (20.13)			15 (9.43)		
Anastomotic leakage	26 (9.89)	14 (5.32)	1 (0.38)	17 (8.25)	6 (2.91)		12 (7.55)	6 (3.77)	1 (0.63)	12 (7.55)	4 (2.52)	
Pulmonary infection	31 (11.79)	28 (10.65)	2 (0.76)	20 (9.71)	21 (10.19)		18 (11.32)	13 (8.18)	2 (1.26)	12 (7.55)	18 (11.32)	
Hydrothorax	41 (15.59)			40 (19.42)			21 (13.21)			30 (18.87)		
Respiratory failure	3 (1.14)	21 (7.98)	2 (0.76)		16 (7.77)		1 (0.63)	11 (6.92)	2 (1.26)		14 (8.81)	
Heart failure	12 (4.56)	7 (2.66)	1 (0.38)	5 (2.43)	1 (0.49)		6 (3.78)	3 (1.89)	1 (0.63)	5 (3.14)	1 (0.63)	
Postoperative hoarseness	9 (3.42)	3 (1.14)		9 (4.37)			4 (2.52)	2 (1.26)		6 (3.77)		
Postoperative bleeding	7 (2.66)	3 (1.14)		10 (4.85)	4 (1.94)		2 (1.26)	1 (0.63)		7 (4.40)	3 (1.89)	
Arrhythmia	8 (3.04)	2 (0.76)		13 (6.31)	3 (1.46)		2 (1.26)	1 (0.63)		10 (6.29)	1 (0.63)	
Pneumothorax	17 (6.46)			13 (6.31)			9 (5.66)			13 (8.18)		
Abnormal liver function	9 (3.42)	1 (0.38)		4 (1.94)	1 (0.49)		3 (1.89)	1 (0.63)		3 (1.89)	1 (0.63)	
Fever	11 (4.18)			5 (2.43)			4 (2.52)			3 (1.89)		
Pulmonary atelectasis	4 (1.52)			8 (3.88)			2 (1.26)			7 (4.40)		
Suspected anastomotic leakage	2 (0.76)			1 (0.49)			1 (0.63)			1 (0.63)		
Chylous fistula	4 (1.52)	3 (1.14)		3 (1.46)	2 (0.97)			3 (1.89)		1 (0.63)	2 (1.26)	
ARDS		5 (1.90)			2 (0.97)			1 (0.63)			2 (1.26)	
Pyothoraxs	2 (0.76)				2 (0.97)		1 (0.63)				2 (1.26)	
Wound.infection	3 (1.14)				2 (0.97)		2 (1.26)				1 (0.63)	
Pulmonary embolism	1 (0.38)		1 (0.38)		1 (0.49)				1 (0.63)		1 (0.63)	
Delirium	1 (0.38)				1 (0.49)		1 (0.63)					
Thrombosis	4 (1.52)			2 (0.97)			1 (0.63)			1 (0.63)		
Ketosis		1.00 (0.38)										
Renal injury	3 (1.14)	1 (0.38)		2 (0.97)	1 (0.49)		1 (0.63)	1 (0.63)		2 (1.26)	1 (0.63)	
Tracheal injury		1 (0.38)	1 (0.38)		1 (0.49)			1 (0.63)	1 (0.63)		1 (0.63)	
Cerebral infarction				1 (0.49)						1 (0.63)		
Gastric perforation					1 (0.49)						1 (0.63)	
Diaphragmatic hernia					1 (0.49)						1 (0.63)	

Fig. 5 Patients with surgical complications (clavien-dindo) above grade 3



10 Risk factors

The univariate analysis for OS revealed that smoking status, cT category, cN category, cTNM stage, surgical approach, thoracic surgical type, complete resection, circumferential resection margin, pathologic differentiation grade, lymphovascular invasion, nerve invasion, pT category, pN category, 8th TNM stage, and grade of postoperative complications (Clavien–Dindo) were significant factors influencing OS. Further multivariate analysis indicated that surgical approach ($P = 0.03$), lymphovascular invasion ($P < 0.001$), pT1 ($P = 0.016$), pT4 ($P = 0.022$), pN3 ($P < 0.001$), pathological stage III ($P = 0.014$), and pathological stage IV ($P = 0.016$) remained significant independent risk factors for OS (Fig. 7A).

For DFS, univariate analysis identified smoking status, cT category, cN category, cTNM stage, thoracic surgical type, complete resection, circumferential resection margin, pathologic differentiation grade, lymphovascular invasion, pT category, pN category, 8th TNM stage, and grade of postoperative complications (Clavien–Dindo) as significant factors. Further multivariate analysis demonstrated that lymphovascular invasion ($P < 0.001$), pT1 ($P = 0.009$), pT2 ($P = 0.019$), pT3 ($P = 0.047$), pN1 ($P = 0.012$), pN2 ($P < 0.001$), pN3 ($P < 0.001$), and pathological stage IV ($P = 0.001$) were significant independent predictors for DFS (Fig. 7B).

11 Discussion

In this study, our data revealed no statistically significant differences in median OS and DFS between the CD and NCD groups, even after adjusting for potential confounders using PSM and IPTW. This indicates that elderly patients with preexisting conditions can still benefit from esophagectomy without a substantial compromise in survival outcomes. The RMST and RMDFS analyses further corroborate these findings, showing comparable outcomes across different subgroups of patients with varying combinations of chronic diseases. The short-term postoperative outcomes also showed no significant differences in the incidence of complications between the CD and NCD groups. Approximately half of the patients experienced grade 3 or higher complications according to the Clavien-Dindo classification, with pulmonary infections, hydrothorax, anastomotic stenosis, and leakage being the most common complications.

The NCD group had a higher incidence of anastomotic stenosis, even after PSM, suggesting that factors other than the measured chronic diseases may contribute to this complication. Conversely, the CD group showed a higher

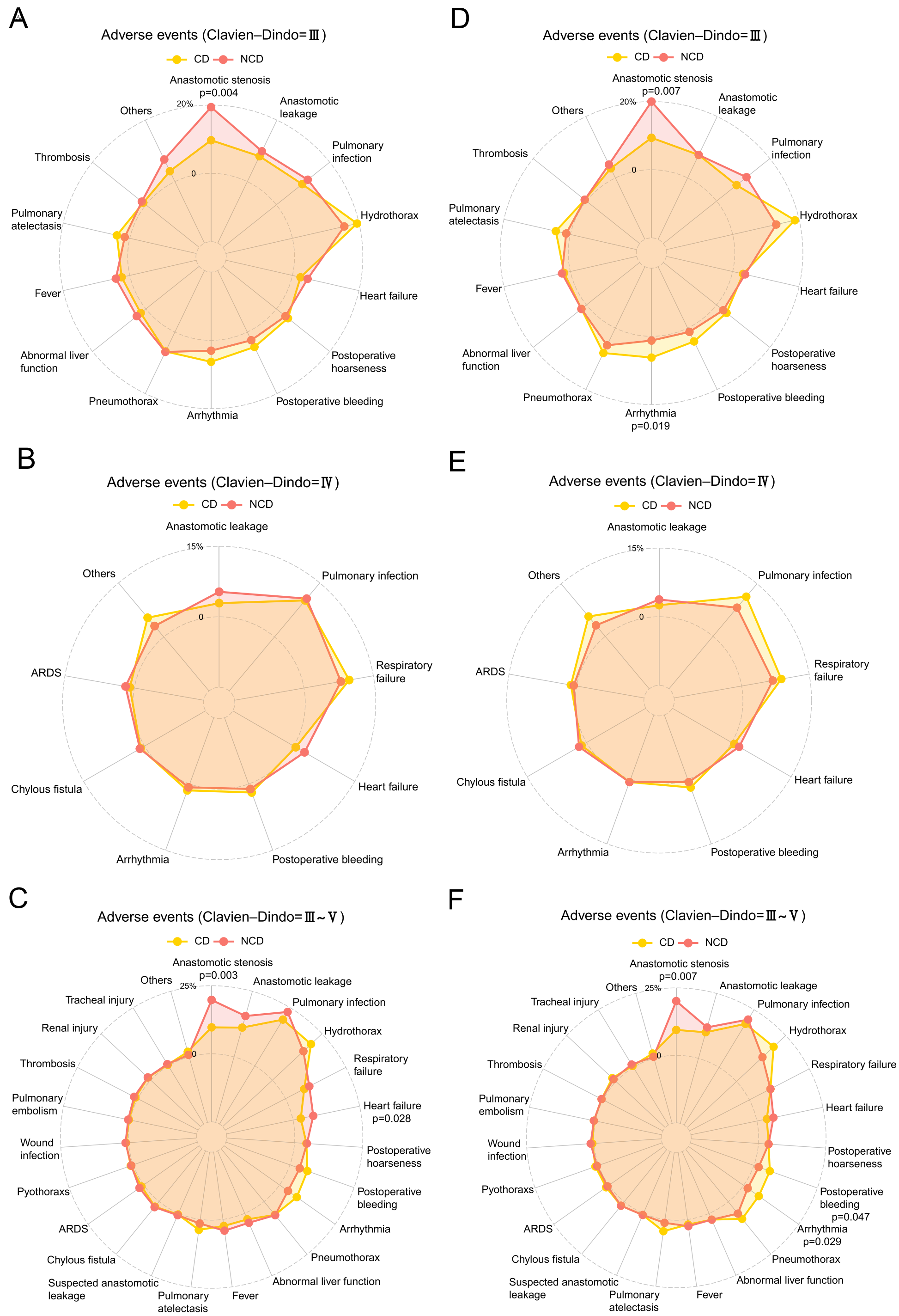


Fig. 6 Adverse events of participants in CD and NCD groups. **A** Clavien-Dindo grade III complications of CD and NCD groups before PSM; **B** Clavien-Dindo grade IV complications of CD and NCD groups before PSM; **C** Clavien-Dindo grade III-V complications of CD and NCD groups before PSM; **D** Clavien-Dindo grade III complications of CD and NCD groups after PSM; **E** Clavien-Dindo grade IV complications of CD and NCD groups after PSM; **F** Clavien-Dindo grade III-V complications of CD and NCD groups after PSM

propensity for arrhythmia and postoperative bleeding, which could be attributed to the underlying cardiovascular conditions prevalent in this group.

Currently, the primary treatment modality for esophageal cancer involves surgery, often combined with chemotherapy, radiotherapy, and immunotherapy as part of a comprehensive treatment approach [28–30]. This paradigm holds true for elderly patients as well. Past research has indicated that elderly patients with esophageal cancer tend to present with more comorbidities compared to their younger counterparts before treatment and experience a higher incidence of complications post-treatment [31–34]. However, studies have shown that surgical treatment offers significantly better OS and DFS rates compared to non-surgical treatment modalities. Moreover, surgical intervention does not markedly increase the incidence of postoperative complications [33–35]. A study pointed out that in patients without underlying

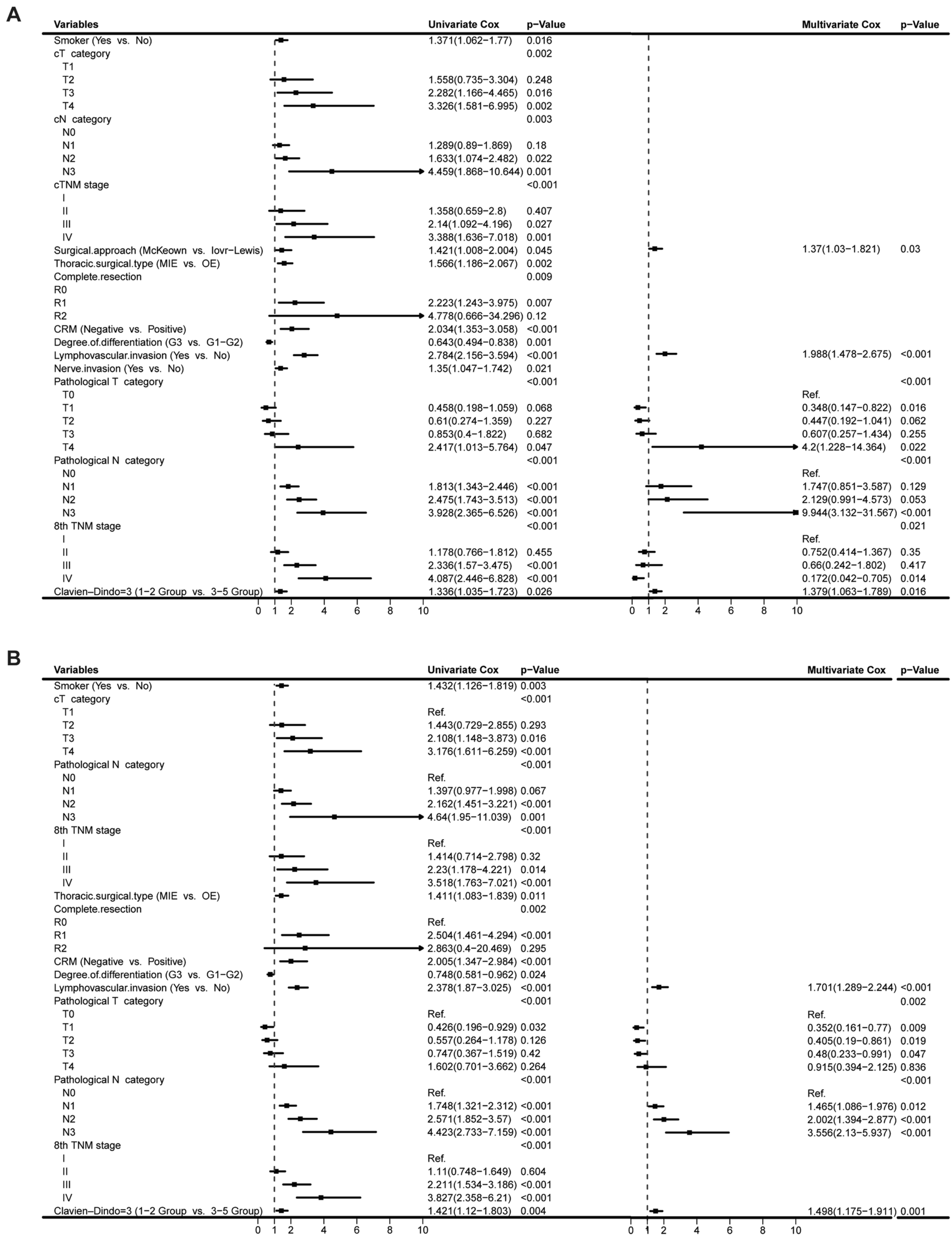


Fig. 7 Univariate and multivariate Cox regression analyses regarding factors affecting OS of patients

diseases, there was no significant difference in the 3-year survival rate between the S (surgical) and NS (non-surgical) groups. However, among patients with complications, the 3-year survival rate was 58% in the S group and 19% in the NS group. For patients with stage II disease, the 3-year survival rate was significantly higher in the S group (72%) compared to the NS group (42%), showing a notable difference in OS. Similarly, for stage III patients, the 3-year survival rate was 56% in the S group versus 36% in the NS group, again indicating a significant OS difference. However, for stage IV patients, no significant difference in 3-year survival rates was observed between the S and NS groups [35]. Further evidence supports the benefit of rigorous surgical screening and rehabilitation programs for elderly patients aged 80 years or older, helping them achieve better survival outcomes. In this group, the median OS was 10 months, while for patients aged between 70 and 80 years, the median OS was 26 months, and for those under 70, the median OS extended to 32 months. Most postoperative deaths occurred within the first 90 days after surgery, with the highest mortality rate seen in the group aged 80 years or older. However, for those patients aged 80 and above who survived beyond 90 days postoperatively, their long-term survival rates were comparable to those of younger patients. This finding underscores the importance of early postoperative survival in determining long-term outcomes, particularly in elderly patients [34,36].

A Japanese study involving 722 patients treated for esophageal cancer categorized the participants into four age groups (< 70 years, 70–75 years, 75–80 years, and ≥ 80 years) to analyze short-term and long-term outcomes post-esophagectomy, as well as differences among treatment groups (preoperative therapy and surgery). The study found that patients aged 80 years or older had significantly lower rates of preoperative chemotherapy compared to the younger age groups. Additionally, the extent of three-field lymph node dissection decreased with increasing age. Elderly patients experienced higher incidences of postoperative cardiovascular and pulmonary complications, although these complications did not correlate with increased mortality rates. The OS rates for patients in the 75–80 years and ≥ 80 years groups were significantly lower than those in the < 70 years group ($P = 0.011$ and $P = 0.002$, respectively) [37]. In 2021, a study conducted by Ji et al. stratified patients by age (< 80 years vs. ≥ 80 years) to assess the impact of concurrent chemoradiotherapy on survival outcomes across various patient profiles33. These findings collectively underscore the importance of individualized treatment strategies for elderly patients with esophageal cancer. They reinforce the notion that a multimodal approach, encompassing surgery, chemotherapy, and radiotherapy, can offer a comprehensive and effective treatment regimen for this patient population.

As research continues to evolve, the treatment paradigms for elderly patients with esophageal cancer are undergoing significant advancements. This study offers valuable insights into the impact of preoperative comorbidities on the prognosis of this patient population. Nonetheless, there remains an urgent need for further exploration into personalized treatment strategies for patients with underlying conditions.

While this study provides valuable insights into the survival outcomes and postoperative complications of elderly patients undergoing esophagectomy for ESCC, several limitations should be noted: At first, as a retrospective cohort study, inherent biases, such as selection bias and information bias, are unavoidable. This design limits the ability to establish causal relationships between preoperative comorbidities and survival outcomes. Then, the study was conducted using data from the SCCH-ECCM database, which may limit the generalizability of the findings to other populations and healthcare settings. Although PSM and IPTW were utilized to adjust for potential confounders, residual confounding may still exist. Variables not accounted for in these models could influence the results. At last,although we investigated the effects of hypertension, diabetes, COPD, and heart disease, our findings suggest that these conditions did not significantly influence survival outcomes within our patient cohort. This may be due to the overall well-managed nature of these comorbidities through pharmacological treatments, which could mask their potential effects on survival. Additionally, the severity of comorbidities in our elderly population may limit the generalizability of our results to other groups with different management strategies or levels of comorbidity severity. Future research should aim to address these limitations by employing prospective, multicenter designs, extending follow-up periods, and incorporating comprehensive quality-of-life assessments. Additionally, more granular analyses of individual comorbidities and treatment modalities are warranted to develop personalized treatment strategies for elderly patients with ESCC.

12 Conclusions

In conclusion, this study emphasizes that advanced age and the presence of basic chronic diseases should not be regarded as absolute contraindications for esophagectomy in elderly patients. Favorable long-term survival outcomes can also be achieved that are comparable to those of patients without such conditions.

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Data availability The datasets supporting the results of the present study can be obtained from the corresponding author upon reasonable request.

Declarations

Competing interests The authors declare no competing interests.

References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. Ca-Cancer J Clin. 2023;1:17–48.
2. Han B, Zheng R, Zeng H, et al. Cancer incidence and mortality in China, 2022. J Natl Cancer Cent. 2024;1:47–53.
3. Kelly RJ, Ajani JA, Kuzdzal J, et al. Adjuvant nivolumab in resected esophageal or gastroesophageal junction cancer. New Engl J Med. 2021;13:1191–203.
4. Shapiro J, van Lanschot J, Hulshof M, et al. Neoadjuvant chemoradiotherapy plus surgery versus surgery alone for oesophageal or junctional cancer (cross): long-term results of a randomised controlled trial. Lancet Oncol. 2015;9:1090–8.
5. Yan X, Duan H, Ni Y, et al. Tislelizumab combined with chemotherapy as neoadjuvant therapy for surgically resectable esophageal cancer: a prospective, single-arm, phase II study (Td-Nice). Int J Surg. 2022;103:106680.
6. Yang H, Liu H, Chen Y, et al. Neoadjuvant chemoradiotherapy followed by surgery versus surgery alone for locally advanced squamous cell carcinoma of the esophagus (Neocrtec5010): a phase III multicenter, randomized open-label clinical trial. J Clin Oncol. 2018;27:2796–803.
7. Kato K, Machida R, Ito Y, et al. Doublet chemotherapy, triplet chemotherapy, or doublet chemotherapy combined with radiotherapy as neoadjuvant treatment for locally advanced oesophageal cancer (jcog1109 next): a randomised, controlled, open-label, phase 3 trial. Lancet. 2024;10447:55–66.
8. Kitagawa Y, Ishihara R, Ishikawa H, et al. Esophageal cancer practice guidelines 2022 edited by the japan esophageal society: part 1. Esophagus-Tokyo. 2023;3:343–72.
9. Gong L, Bai M, Dai L, et al. Caca guidelines for holistic integrative management of esophageal carcinoma. Holistic Integr Oncol. 2023;1:34.
10. Li K, Lu S, Li C, et al. Long-term outcomes of smoker and drinker with oesophageal squamous cell carcinoma after oesophagectomy: a large-scale propensity score matching analysis. Bmj Open Gastroenter. 2024;1:e001452.
11. Shinozuka T, Kanda M, Shimizu D, et al. Prognostic value of a modified albumin-bilirubin score designed for patients with esophageal squamous cell carcinoma after radical resection. Ann Surg Oncol. 2022;8:4889–96.
12. Deboever N, Jones CM, Yamashita K, Ajani JA, Hofstetter WL. Advances in diagnosis and management of cancer of the esophagus. Brit Med J. 2024. https://doi.org/10.1136/bmj-2023-074962.
13. MacGuill M, Mulligan E, Ravi N, et al. Clinicopathologic factors predicting complete pathological response to neoadjuvant chemoradiotherapy in esophageal cancer. Dis Esophagus. 2006;4:273–6.
14. Wang M, Miao H. Disease burden and related risk factors of esophageal cancer in china and globally from 1990 to 2021, with forecast to 2035: an analysis and comparison. Tob Induc Dis. 2024.

15. Li Y, Xu J, Gu Y, Sun X, Dong H, Chen C. The disease and economic burdens of esophageal cancer in China from 2013 to 2030: dynamic cohort modeling study. Jmir Public Hlth Sur. 2022;3: e33191.
16. Jiang Q, Shu Y, Jiang Z et al. Burdens of stomach and esophageal cancer from 1990 to 2019 and projection to 2030 in China: findings from the 2019 global burden of disease study. J Glob Health. 2024; 4025.
17. Global, Regional, and National Burden of Diseases and Injuries for Adults 70 Years and Older: Systematic Analysis for the Global Burden of Disease 2019 Study. Bmj-Brit Med J. 2022; e68208.
18. Worrell SG, Alvarado CE, Thibault D, et al. Impact of diabetes on pathologic response to multimodality therapy for esophageal cancer. Ann Thorac Surg. 2024;1:190–6.
19. Rong Y, Hao Y, Wei D, et al. Association between preoperative anxiety states and postoperative complications in patients with esophageal cancer and COPD: a retrospective cohort study. BMC Cancer. 2024;1:606.
20. Lee JE, Han K, Yoo J, et al. Association between metabolic syndrome and risk of esophageal cancer: a nationwide population-based study. Cancer Epidem Biomar. 2022;12:2228–36.
21. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (Strobe) statement: guidelines for reporting observational studies. Bmj-Brit Med J. 2007;7624:806–8.
22. Ajani JA, D'Amico TA, Bentrem DJ, et al. Esophageal and esophagogastric junction cancers, version 2.2023, Nccn clinical practice guidelines in oncology. J Natl Compr Cancer Ne. 2023;4:393–422.
23. Obesity epidemic puts millions at risk from related diseases. Isr J Med Sci. 1997; 10: 706.
24. James WP. Who recognition of the global obesity epidemic. Int J Obesity. 2008; S120–6.
25. Low DE, Alderson D, Cecconello I, et al. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (Eccg). Ann Surg. 2015;2:286–94.
26. Bolliger M, Kroehnert JA, Molineus F, Kandioler D, Schindl M, Riss P. Experiences with the standardized classification of surgical complications (Clavien-Dindo) in General Surgery Patients. Eur Surg. 2018;6:256–61.
27. Katayama H, Kurokawa Y, Nakamura K, et al. Extended clavien-dindo classification of surgical complications: Japan Clinical Oncology Group postoperative complications criteria. Surg Today. 2016;6:668–85.
28. Yang Y, Liu J, Liu Z, et al. Two-year outcomes of clinical N2–3 esophageal squamous cell carcinoma after neoadjuvant chemotherapy and immunotherapy from the phase 2 nice study. J Thorac Cardiov Sur. 2024;3:838–47.
29. Lee Y, Samarasinghe Y, Lee MH, et al. Role of adjuvant therapy in esophageal cancer patients after neoadjuvant therapy and esophagectomy: a systematic review and meta-analysis. Ann Surg. 2022;1:91–8.
30. McKay SC, Louie BE, Molena D, et al. Tumor differentiation impacts response to neoadjuvant therapy and survival in patients with esophageal adenocarcinoma. J Thorac Cardiov Sur. 2024;6:1943–50.
31. Matsuda S, Kitagawa Y, Okui J, et al. Old age and intense chemotherapy exacerbate negative prognostic impact of postoperative complication on survival in patients with esophageal cancer who received neoadjuvant therapy: a nationwide study from 85 japanese esophageal centers. Esophagus-Tokyo. 2023;3:445–54.
32. Rompen IF, Crnovrsanin N, Nienhuser H, et al. Age-dependent benefit of neoadjuvant treatment in adenocarcinoma of the esophagus and gastroesophageal junction: a multicenter retrospective observational study of young versus old patients. Int J Surg. 2023;12:3804–14.
33. Ji Y, Du X, Zhu W, et al. Efficacy of concurrent chemoradiotherapy with s-1 vs radiotherapy alone for older patients with esophageal cancer: a multicenter randomized phase 3 clinical trial. JAMA Oncol. 2021;10:1459–66.
34. Motoyama S, Maeda E, Iijima K, et al. Does esophagectomy provide a survival advantage to patients aged 80 years or older? analyzing 5066 patients in the national database of hospital-based cancer registries in Japan. Ann Surg. 2022;1:e16-23.
35. Li K, Li C, Nie X, et al. Surgical vs nonsurgical treatment for esophageal squamous cell carcinoma in patients older than 70 years: a propensity score matching analysis. J Gastrointest Surg. 2024;5:611–20.
36. Cooper L, Orgad R, Levi Y, et al. Esophageal cancer in octogenarians: should esophagectomy be done? J Geriatr Oncol. 2024;2: 101710.
37. Miyata H, Yamasaki M, Makino T et al. Clinical outcome of esophagectomy in elderly patients with and without neoadjuvant therapy for thoracic esophageal cancer. Ann Surg Oncol. 2015; S794–801.