AHOT Acta Haematologica Oncologica Turcica

Acta Haematol Oncol Turc 2026;59(2):112-119

Original Article

DOI: 10.4274/ahot.galenos.2026.2026-4-6

Quantifying the Survival Benefit of Trimodality Therapy in Esophageal Squamous Cell Carcinoma: An IPTW-adjusted Retrospective Analysis

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ABSTRACT

Aim: The survival advantage of surgery following chemoradiotherapy in esophageal squamous cell carcinoma (ESCC) remains debated due to potential selection bias in non-randomized studies. We aimed to quantify the magnitude of survival benefit associated with trimodality therapy after rigorous adjustment for baseline imbalances.

Methods: We retrospectively analyzed 54 patients with stage II-III ESCC treated between 2022 and 2025. Patients received either neoadjuvant chemoradiotherapy followed by surgery (trimodality group, n=24) or definitive chemoradiotherapy alone (dCRT group, n=30). To address treatment selection bias, inverse probability of treatment weighting (IPTW) based on propensity scores was applied. Progression-free survival (PFS) and overall survival (OS) were evaluated using weighted Kaplan-Meier estimates and Cox proportional hazards models.

Results: At a median follow-up of 23.5 months, trimodality therapy was associated with a substantially prolonged PFS compared with dCRT (median 67.6 vs. 9.2 months, p=0.007). Similarly, OS was significantly improved (median 72.1 vs. 16.6 months, p=0.009). In multivariable analysis, surgery remained independently associated with improved OS [hazard ratio (HR): 0.41, 95% confidence interval (CI): 0.22-0.78, p=0.006] and PFS (HR: 0.44, 95% CI: 0.24-0.81, p=0.008). These findings were consistent after IPTW adjustment (OS HR: 0.46; PFS HR: 0.49, both p<0.01), indicating a robust and clinically meaningful survival benefit.

Conclusion: After rigorous adjustment for baseline differences, trimodality therapy was associated with a substantial survival advantage over dCRT in patients with locally advanced ESCC. These findings suggest that the magnitude of benefit with surgery may be greater than previously appreciated in real-world populations, supporting its use in appropriately selected patients.

Keywords: Cancer research, cell therapy, chemotherapy, clinical hematology, clinical oncology, clinical trials

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Received: 05.05.2026 **Accepted:** 05.06.2026 **Epub:** 29.07.2026 **Publication Date:** 21.08.2026

Cite this article as: Dilli İ, Kavak EE, Sütçüoğlu O, et al. Quantifying the survival benefit of trimodality therapy in esophageal squamous cell carcinoma: an IPTW-adjusted retrospective analysis. Acta Haematol Oncol Turc. 2026;59(2):112-119

Introduction

Esophageal cancer is considered to be one of the most aggressive malignancies on a global scale [1]. esophageal squamous cell carcinoma (ESCC) is the predominant histologic subtype in Eastern and Central Asia, and it also constitutes a major proportion of esophageal cancers in some regions of Türkiye [2]. Despite advances in multimodal treatment strategies, long-term survival remains poor, with 5-year survival rates rarely exceeding 25%, largely due to the high prevalence of locally advanced disease at diagnosis [3].

For patients with stage II-III ESCC, multimodality treatment has become the cornerstone of care [4]. Neoadjuvant chemoradiotherapy followed by surgery (trimodality therapy) is widely considered the standard approach for resectable disease, largely based on randomized trials such as the CROSS study, which demonstrated improved overall survival (OS) compared with surgery alone [5]. However, the role of surgery following chemoradiotherapy remains controversial, particularly when compared with definitive chemoradiotherapy (dCRT), which is often used in patients deemed medically inoperable or with tumors of borderline resectability.

Several studies have attempted to compare trimodality therapy with dCRT, but the interpretation of these findings is inherently limited by treatment selection bias [6]. Patients undergoing surgery are typically younger, have better performance status, and present with less advanced disease, making it difficult to determine whether observed survival differences reflect a true treatment effect or simply differences in baseline characteristics [7-9]. Even in studies employing multivariable adjustment, residual confounding remains a major concern.

Therefore, a critical unresolved question is not only whether surgery improves survival, but also to what extent the observed benefit reflects a true therapeutic effect rather than patient selection. Quantifying this distinction is essential for optimizing treatment decisions in real-world clinical practice.

In this context, we conducted a retrospective analysis of patients with locally advanced ESCC who were treated at a high-volume tertiary center. Using inverse probability of treatment weighting (IPTW) to minimize baseline imbalances, we aimed to quantify the magnitude of the survival benefit associated with trimodality therapy compared with dCRT.

Methods

Study Design and Patient Selection

This retrospective, single-center cohort study was conducted in the Department of Medical Oncology at University of Health Sciences Türkiye, Ankara Etlik City Hospital and included patients diagnosed with locally advanced ESCC between January 2022 and March 2025. The study was approved by the University of Health Sciences Türkiye, Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee No. 1 (approval no: AEŞH-BADEK1-2025-694, date: 17.12.2025). It was conducted in accordance with the Helsinki Declaration.

Patients were identified through the institutional oncology database. Eligibility criteria included: histopathologically confirmed ESCC, clinical stage II-III disease according to the American Joint Committee on Cancer 8th edition staging system [10], completion of definitive or neoadjuvant CRT and availability of follow-up and survival data. Exclusion criteria were the presence of distant metastasis (M1disease), histological subtypes other than squamous cell carcinoma, prior thoracic radiotherapy or systemic chemotherapy for another malignancy, and incomplete clinical or survival data.

Clinical staging was based on endoscopic ultrasound [11], contrast-enhanced computed tomography (CT), and/or positron emission tomography-CT (PET-CT). Patients with incomplete staging data were categorized as having "unknown" clinical- stage variables.

To address missing stage information, the clinical T (cT) and clinical N (cN) variables were incorporated into multivariate Cox regression models using dummy coding, with "unknown" included as a separate category. Sensitivity analyses excluding patients with unknown cT values were also performed to assess the robustness of the results.

Treatment Groups

Patients were categorized into two groups based on treatment strategy and operability:

1. Trimodality (Surgery) Group: Patients who received neoadjuvant CRT followed by curative-intent esophagectomy.

2. Definitive CRT Group: Patients treated with definitive CRT without surgery due to medical inoperability, advanced local invasion, or patient refusal.

Decisions regarding surgical eligibility were made by a multidisciplinary tumor board consisting of medical oncologists, radiation oncologists, thoracic surgeons, and radiologists.

Chemoradiotherapy Protocol

All patients received concurrent CRT with curative intent over a 5-6- week period.

Chemotherapy: Weekly carboplatin (area under the curve: 2, day 1) combined with paclitaxel (50 mg/m^2, day 1) administered concurrently radiotherapy.

Radiotherapy: External-beam radiotherapy was delivered to a total dose of 50.4-60 Gy in daily fractions of 1.8-2.0 Gy over 5-6 weeks, using three-dimensional conformal or intensity-modulated radiotherapy techniques. This dose range is consistent with commonly accepted standard-dose dCRT schedules, which have been shown to provide an optimal balance between efficacy and treatment-related toxicity [12].

In the neoadjuvant setting, surgical resection was planned 6-8 weeks after completion of CRT, provided an adequate clinical response and an acceptable performance status [Eastern Cooperative Oncology Group (ECOG) 0-2].

Surgical Approach and Pathologic Assessment

Patients in the trimodality group underwent transthoracic or transhiatal esophagectomy with regional lymph node dissection. The surgical approach (Ivor-Lewis or McKeown procedures) was determined based on tumor location and the surgeon's discretion. Pathological evaluation included assessment of resection margin status (R0/R1), pathological tumor and pathological nodal stage, and treatment response. Pathological complete response was defined as the absence of residual viable tumor cells in the resected specimen.

Data Collection and Variables

Demographic, clinical, treatment-related, and pathological data were retrospectively collected from electronic medical records. Collected variables included age, sex, smoking status, comorbidities, primary tumor localization, cT and cN stage, treatment modality, radiation dose, number of chemotherapy cycles, progression-free survival (PFS), and OS.

Outcome Definitions and Follow-up

OS was defined as the time from the initiation of chemoradiotherapy (day 1 of treatment) to death from any cause.

PFS was defined as the time from the same starting point to the first documented disease progression or death, whichever occurred first.

For patients undergoing surgery, postoperative recurrence or death was considered a PFS event.

Patients who were alive and progression-free at the last follow-up were censored on that date.

Sensitivity analyses were repeated using the date of diagnosis as time zero, yielding consistent results.

Patients were followed every 3 months during the first 2 years and every 6 months thereafter. Disease recurrence was confirmed by imaging (CT or PET-CT) and/or by endoscopic biopsy.

Statistical Analysis

Survival outcomes were estimated using the Kaplan-Meier method and compared with the log-rank test. Multivariable Cox proportional hazards regression models were used to assess the independent association between surgery and survival outcomes, adjusting for age, sex, cT stage, cN stage, tumor location, ECOG performance status, and treatment modality. The proportional hazards assumption was verified using Schoenfeld residuals. To further control for treatment selection bias, IPTW based on propensity scores was performed. Propensity scores were estimated using logistic regression incorporating the same covariates. Covariate balance before and after weighting was assessed using standardized mean differences (SMDs), with values <0.10 indicating adequate balance (Supplementary Table 1). Weighted Kaplan-Meier curves and weighted Cox regression models were generated to estimate adjusted hazard ratios (HRs). A two-sided p value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 30.0 and BluSky Statistics (version 10.3.2).

Results

A total of 54 patients with locally advanced ESCC were included in the analysis. Of these, 24 patients (44.4%) underwent chemoradiotherapy followed by surgery (trimodality group), while 30 patients (55.6%) underwent dCRT group.

Patient Characteristics

Baseline demographic and clinical characteristics by treatment modality are summarized in Table 1. The median age of the entire cohort was 62.0 years (range, 36.0-86.0). Female patients constituted 52% of the study population; no statistically significant difference in sex distribution was observed between the treatment groups (p=0.161). Most patients (88.9%) were active smokers, and smoking status did not differ significantly between groups (p=0.561).

The primary tumor's location was found to be most commonly in the upper thoracic region in both cohorts (41.7% in the trimodality group vs 60.0% in the dCRT group), with no statistically significant difference (p=0.381).

Incomplete clinical staging data were present for 39% of patients. The absence of cT stage data was observed more frequently in the dCRT group than in the trimodality group (83.3% vs. 58.3%). Baseline differences between patients with known and unknown cT stage are summarized in Supplementary Table 2. In the sensitivity analysis restricted to patients with known cT stage (n=25), surgery remained significantly associated with improved OS (median 70.4 vs. 17.1 months, p=0.018) and PFS (p=0.021).Thus, the impact of surgery on survival was consistent even after excluding patients with incomplete staging.

cT stage differed significantly between groups (p=0.004). Early T1-T2 stages were observed only in the surgical cohort, whereas T4 disease was present exclusively in patients who did not undergo surgery. cN stage showed a near-significant difference (p=0.054), with a higher proportion of N3 disease in the surgical group (43.5% vs. 10.0%). The proportion receiving concurrent chemoradiotherapy was comparable between the surgical and non-surgical groups (70.8% vs. 80.0%, p=0.434).

Postoperative Outcomes and Recurrence Patterns

Among the 24 patients who underwent surgery, no postoperative mortality occurred within 90 days.

During follow-up, 12 patients (50.0%) in the surgery group and 25 patients (83.3%) in the definitive CRT group experienced disease recurrence or progression. In the surgical group, recurrence was predominantly distant metastasis (8 patients, 66.7%), whereas locoregional recurrence occurred in 4 patients (33.3%).

Conversely, patients treated with definitive CRT had a higher proportion of locoregional failures (16 patients, 64.0%) and a lower proportion of distant relapses (9 patients, 36.0%).

Table 1. Baseline demographic and clinical characteristics of patients according to surgical status

Variable	Category	Surgery (n=24) n	%	No surgery (n=30) n	%	p value
Gender	Female	15	62.5	13	43.3	0.161
	Male	9	37.5	17	56.7	
Smoking status	Smoker	22	91.7	26	86.7	0.561
	Never	2	8.3	4	13.3	
	Former (quitted)	0	0.0	0	0.0	
Primary tumor location	Upper thoracic	10	41.7	18	60.0	0.381
	Middle thoracic	8	33.3	6	20.0	
	Esophagogastric junction	6	25.0	6	20.0	
Clinical T stage (cT)	Unknown	14	58.3	25	83.3	**0.004**
	T1	3	12.5	0	0.0	
	T2	6	25.0	0	0.0	
	T3	1	4.2	1	3.3	
	T4	0	0.0	4	13.3	
Clinical N stage (cN)	Unknown	1	4.3	3	10.0	0.054
	N0	6	26.1	9	30.0	
	N1	5	21.7	9	30.0	
	N2	1	4.3	6	20.0	
	N3	10	43.5	3	10.0	
Concurrent chemoradiotherapy	Yes	17	70.8	24	80.0	0.434
	No	7	29.2	6	20.0	

The median interval to disease recurrence was 15.2 months after surgery, compared with 8.4 months after definitive CRT.

These findings indicate that surgery improves locoregional control, whereas systemic relapse remains the primary mode of failure in both groups (Table 2).

Progression-free and OS

When chemoradiotherapy initiation was used as the common time-zero point, the median PFS and OS remained significantly longer in the surgery group. A sensitivity analysis using the date of diagnosis as time zero yielded similar findings, confirming that differences in survival were not explained by time-definition bias.

At a median follow-up of 23.5 months, median PFS for the cohort was 19.9 months (95% CI: 0.7-39.0). Patients who underwent surgery had significantly longer PFS than those treated with dCRT (67.6 months, 95% CI: 17.8-117.4 vs. 9.2 months, 95% CI: 4.9-13.4; p=0.007, log-rank test) (Figure 1). Survival comparisons were performed using the log-rank test. Median OS and PFS values are shown with 95% confidence intervals.

Patients who underwent neoadjuvant chemoradiotherapy followed by surgery had significantly longer PFS than those treated with dCRT (median PFS: 67.6 vs. 9.2 months, p=0.007, log-rank test).

Similarly, OS was significantly longer in the surgical cohort (72.1 months, 95% CI: 24.9-119.2) than in the dCRT group (16.6 months, 95% CI: 7.2-25.9; p=0.009, log-rank test) (Figure 2).

Table 2. Postoperative mortality and recurrence patterns

Outcome	Surgery group (n=24)	Definitive CRT (n=30)	p value
90-day mortality	0 (0.0%)	3 (10.0%)	0.091
Any recurrence/progression	12 (50.0%)	25 (83.3%)	0.007
Locoregional recurrence	4 (33.3%)	16 (64.0%)	0.028
Distant metastasis	8 (66.7%)	9 (36.0%)	0.042
Median time to recurrence (months)	15.2 (95% CI: 9.8-20.7)	8.4 (95% CI: 5.6-11.2)	0.01

Recurrence patterns were categorized as locoregional (tumor bed, anastomotic site, or regional lymph nodes) and distant (lung, liver, bone, or non-regional lymph nodes)
CRT: Chemoradiotherapy, CI: Confidence interval

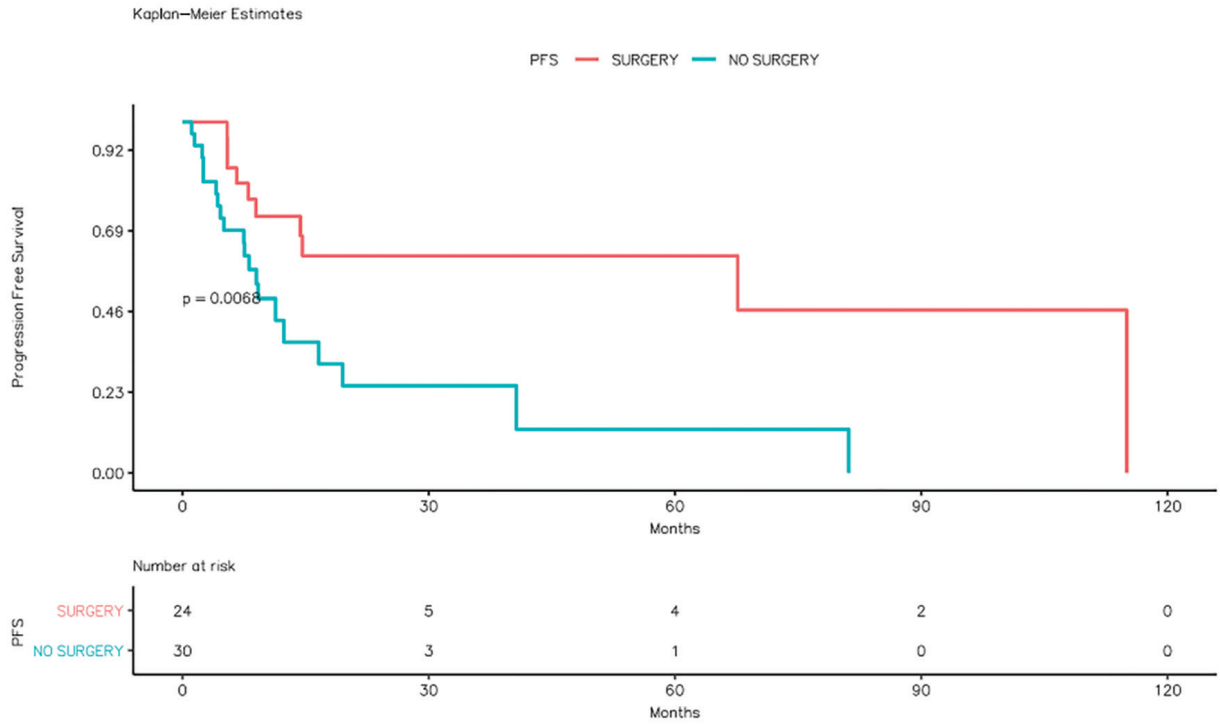

Figure 1. Kaplan-Meier curves for overall survival and PFS in patients with locally advanced esophageal squamous cell carcinoma treated with chemoradiation followed by surgery (blue line) or definitive chemoradiation (red line)
PFS: Progression-free survival

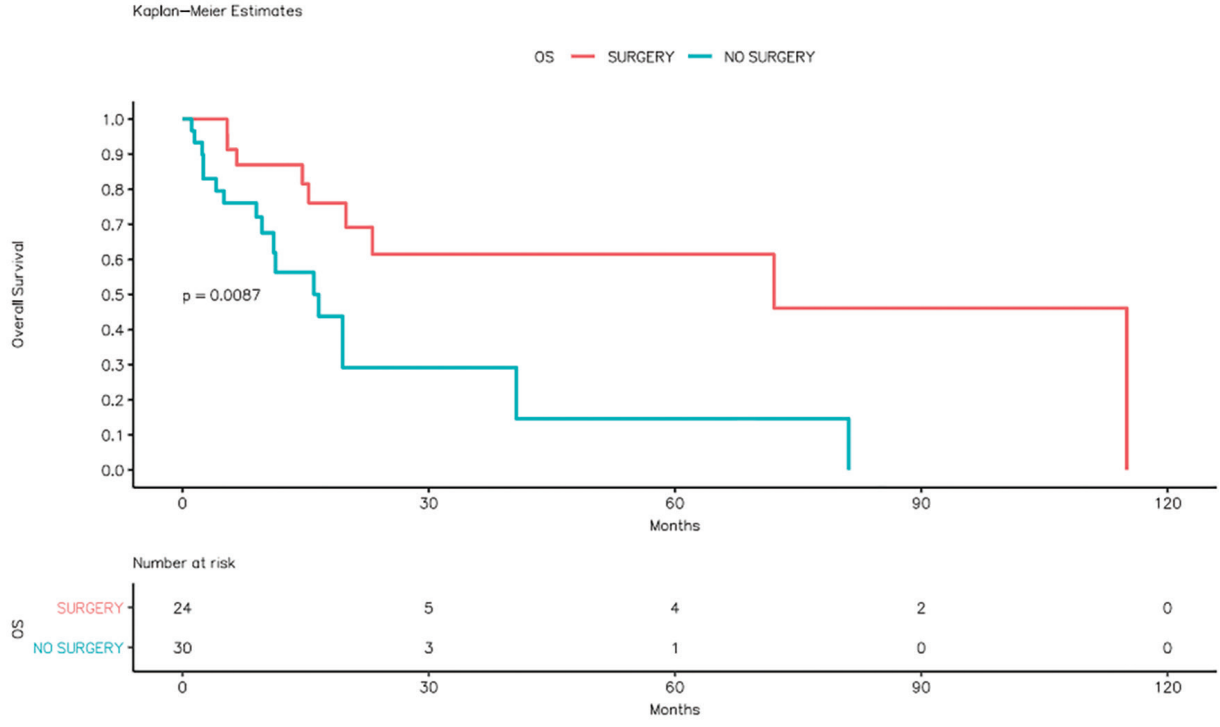

Figure 2. Kaplan-Meier curve for OS in patients with locally advanced ESCC according to treatment modality
OS: Overall survival, ESCC: Esophageal squamous cell carcinoma

Adjusted Survival Analyses

In the 90-day landmark analysis (excluding three early deaths in the definitive CRT group), surgery remained significantly associated with improved survival (landmark OS: median 72.1 vs. 15.8 months, p=0.012).

In multivariate Cox regression analysis, after adjustment for age, sex, cT, cN, tumor site, ECOG PS, and concurrent CRT, surgery was an independent predictor of longer OS (HR: 0.41, 95% CI: 0.22-0.78, p=0.006) and PFS (HR: 0.44, 95% CI: 0.24-0.81, p=0.008).

After weighting, all covariates achieved adequate balance (all SMDs <0.10), confirming successful adjustment for baseline differences between groups (Supplementary Table 1). Weighted analyses confirmed a consistent benefit of surgery, with IPTW-adjusted HRs of 0.46 for OS and 0.49 for PFS (both p<0.01). These findings were concordant with the unadjusted Kaplan-Meier results, supporting the robustness of the observed survival advantage. Adjusted analyses are summarized in Table 3.

Discussion

In this real-world cohort of patients with locally advanced ESCC, we found that trimodality therapy was associated with a substantial and consistent survival advantage compared with dCRT. Importantly, this association remained robust across multiple analytical approaches, including multivariable adjustment, propensity score-based weighting, and landmark analysis. These findings suggest that the observed survival benefit is unlikely to be solely explained by baseline imbalances between treatment groups.

A key challenge in interpreting comparative studies between trimodality therapy and dCRT is the presence of treatment selection bias. Patients selected for surgery are inherently more likely to have favorable clinical characteristics, including better performance status and lower tumor burden. As a result, the magnitude of benefit attributed to surgery is often questioned. Our study aimed to minimize this bias and more accurately estimate the independent association between treatment strategy and survival by applying IPTW. Notably, the consistency between unadjusted and weighted analyses conducted in our cohort suggests that the association between surgery and improved survival persisted after adjustment for measured baseline differences (Supplementary Table 1).

While previous randomized and observational studies have suggested a survival benefit with trimodality therapy, most have focused on demonstrating superiority rather than quantifying the magnitude of benefit under real-world conditions. In this context, our findings provide clinically relevant estimates of improvement in survival after adjustment for confounding factors. The observed hazard reductions for both OS and PFS indicate that the effect size associated with surgery is not only statistically significant but also clinically meaningful [13,14].

In our cohort, the median OS for patients treated with surgery after chemoradiotherapy was 72.1 months, compared with 16.6 months for the dCRT group (p=0.009). Similarly, the median PFS was significantly longer in the surgical group (67.6 vs. 9.2 months, p=0.007). These results indicate that surgical resection, when feasible, provides a substantial survival benefit beyond local control.

The higher proportion of patients with unknown cT stage in the non-surgical group likely reflects diagnostic limitations among patients with poor performance status or advanced local invasion, both of which preclude endoscopic evaluation. Although staging heterogeneity is a limitation of retrospective datasets, our sensitivity analysis confirmed that the survival benefit associated with surgery persisted even after excluding patients with incomplete staging data, thereby supporting the robustness of our findings.

The CROSS trial firmly established neoadjuvant CRT followed by surgery as the standard of care for resectable ESCC, reporting a median OS of 49 months in the CRT-surgery arm compared with 24 months for surgery alone, and an R0 resection rate of 92% [5]. Our study extends these observations by comparing trimodality therapy with definitive chemoradiation, showing that even in a real-world cohort, the addition of surgery remains prognostically favorable. All survival endpoints were measured from the initiation of chemoradiotherapy to ensure consistent time-zero definitions between treatment groups. This approach minimizes bias arising from treatment-related delays or differences in the timing of surgery. A sensitivity analysis using the date of diagnosis as time-zero produced similar results, confirming that the observed survival advantage was not affected by temporal definition bias. This aligns with the findings of Teoh et al. [7], who reported improved long-term outcomes with surgery compared to definitive CRT in resectable squamous carcinoma of the esophagus.

Table 3. Adjusted survival analyses according to treatment approach

Analysis type	Model adjustment	Endpoint	HR (95% CI)	p value
Multivariate Cox	Adjusted for age, sex, cT, cN, tumor site, ECOG PS, and concurrent CRT	Overall survival	0.41 (0.22-0.78)	0.006
		Progression-free survival	0.44 (0.24-0.81)	0.008
IPTW-weighted Cox	IPTW based on propensity scores	Overall survival	0.46 (0.28-0.75)	<0.01
		Progression-free survival	0.49 (0.30-0.79)	<0.01
90-day Landmark	Early deaths within 90 days excluded	Overall survival	Median 72.1 vs. 15.8 months	0.012

ECOG: Eastern Cooperative Oncology Group, CRT: Chemoradiotherapy, IPTW: Inverse probability of treatment weighting, HR: Hazard ratio, PS: Performance status, CI: Confidence interval, cT: Clinical T, cN: Clinical N

Conversely, the Fédération Francophone de Cancérologie Digestive 9102 trial reported no significant OS difference between surgery and definitive chemoradiation, although the trial was limited by high treatment-related mortality (11%) and older radiotherapy techniques [6]. More contemporary analyses, including real-world data from Asia, have consistently shown that surgery following CRT leads to better local control and survival outcomes in fit patients [15-17]. Qian et al. [18] reported that among patients with locally advanced ESCC who achieved a clinical CR after chemoradiotherapy, dCRT resulted in OS outcomes comparable to those observed with trimodality therapy. These findings suggest that omission of surgery may represent a reasonable treatment strategy in carefully selected patients who have a favorable response to chemoradiotherapy, supporting a more individualized, response-adapted treatment approach.

A substantial systematic review and meta-analysis, encompassing over 3,000 patients, has indicated that those subjected to neoadjuvant CRT followed by surgery exhibited considerably elevated 3- and 5-year survival rates in comparison with those undergoing definitive CRT (HR=0.63, p<0.001) [8]. Similarly, Lin et al. [16] showed that trimodality therapy resulted in superior locoregional control and OS in thoracic ESCC, particularly among younger and fit patients. A more recent Asian multicenter retrospective study by Zhang et al. [17] also demonstrated that patients who were initially unresectable (T4) but downstaged after CRT and underwent surgery achieved significantly improved OS and disease-free survival compared to those who received CRT alone. Collectively, these studies support the concept that surgery remains a key determinant of long-term disease control in operable patients.

Tumor characteristics, especially tumor depth, emerged as significant prognostic determinants in our cohort. Patients with T1-T2 tumors predominated in the surgery group, whereas T4 disease was limited to non-surgical cases, underscoring the role of locoregional invasion in determining operability. The near-significant trend in cN status suggests that extensive nodal involvement may still be compatible with resection, particularly in patients achieving nodal response after CRT. This is consistent with previous data indicating that pCR and nodal downstaging are strong prognostic indicators following neoadjuvant CRT [8,16].

Despite the observed benefits of surgery, definitive CRT remains a crucial curative-intent option for medically inoperable patients or those unwilling to undergo esophagectomy [19,20]. In our study, over half of the cohort received definitive CRT, reflecting the real-world challenges of comorbidities, frailty, and patient preference [21]. Importantly, advances in radiation techniques, such as proton beam therapy and image-guided intensity-modulated radiation therapy, have reduced toxicity while improving local control [22]. Nevertheless, radiation dose escalation beyond standard definitive doses remains controversial. A recent systematic review and meta-analysis by Wang et al. [12] demonstrated that higher radiation doses did not translate into consistent survival benefits, while being associated with increased treatment-related toxicity, supporting the continued use of standard-dose regimens (approximately 50-50.4 Gy) in dCRT for esophageal cancer. Furthermore, the integration of immune checkpoint inhibitors (e.g., PD-1/PD-L1 blockade) into the CRT setting has shown promising results, potentially redefining the future standard of care for both definitive and neoadjuvant approaches [23,24]. Early-phase trials combining CRT with immunotherapy agents such as nivolumab and camrelizumab have demonstrated encouraging response rates and manageable toxicity profiles [25].

To mitigate potential selection and immortal time biases inherent to retrospective analyses, we performed complementary statistical adjustments, including a 90-day landmark analysis, multivariate Cox regression, and propensity score-based weighting. Each approach consistently confirmed that surgery after chemoradiotherapy remained independently associated with superior OS and PFS. These findings strengthen the validity of our results and suggest that the survival benefit observed for trimodality therapy is not solely attributable to baseline differences in patient fitness or tumor stage.

Importantly, definitive CRT remains a valuable curative-intent option for patients who are medically inoperable or who decline surgery. In our cohort, approximately half of the patients received non-surgical treatment, reflecting real-world constraints related to patient comorbidity and preferences. Technological advances in radiotherapy delivery and immunotherapy combinations may further improve the efficacy of definitive CRT.

Study Limitations

This study has several limitations inherent to its retrospective and single-center design. The relatively small sample size and the specific referral patterns in our region, where ESCC is highly prevalent, may limit the generalizability of the findings. Nevertheless, the inclusion of all consecutive patients and the use of robust adjustment methods (multivariate and IPTW analyses) mitigate selection and information bias to a considerable extent. Moreover, our real-world data reflect clinical practice patterns from a high-incidence area in eastern Turkey and provide unique insights into the management of locally advanced ESCC in resource-limited settings.

These results may inform multidisciplinary decision-making in similar populations, particularly the choice between trimodality therapy and definitive CRT.

Conclusion

After bias-adjusted analyses, surgery was consistently associated with improved survival outcomes in this cohort. Surgical resection should be considered whenever feasible within a multidisciplinary treatment strategy. Definitive CRT remains an appropriate curative-intent option for selected patients who are not surgical candidates. Larger prospective studies are warranted to further refine patient selection and optimize multimodal treatment approaches.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Türkiye, Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee No. 1 (approval no: AEŞH-BADEK1-2025-694, date: 17.12.2025).

Informed Consent: This retrospective study.

Footnotes

Authorship Contributions

Concept: İ.D., E.E.K., O.S., Ö.A.İ., G.K., G.İ.İ., Ş.E., Design: İ.D., E.E.K., G.İ.İ., D.Y., Data Collection or Processing: İ.D., E.E.K., D.Y., M.T.B., S.D.Ş., Ş.E., A.T.A., Y.G., G.Y., D.M.K., Analysis or Interpretation: İ.D., E.E.K., D.Y., F.A., Y.G., D.M.K., Literature Search: İ.D., G.K., Ş.E., Y.G., G.Y., D.M.K., Writing: İ.D.,Ö.A.İ., B.A., M.T.B., S.D.Ş., Ş.E.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Supplementary Tables: https://d2v96fxpocvxx.cloudfront.net/d363ec1e-9e5e-4591-a00a-d656bfcabb80/content-images/bc33ff9e-87f2-460a-87bb-54435150cb41.pdf

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