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Real-world Outcomes of Chemoradiotherapy with or Without Surgery in Locally Advanced Esophageal Cancer: A Retrospective Analysis

Anisa Aljabri[1,2], Abdulla Alzibdeh[1], Mohammed Qambar[1], Soha Salem[3,4], Omar Khader[1], Fawzi Abuhijla[1], Sara Mheid[1], Ayah Erjan[1], Issa Mohamad[1], Jamal Khader[1]

[1]King Hussein Cancer Center (KHCC), Department of Radiation Oncology, Amman, Jordan
[2]Royal Hospital, National Oncology Center, Department of Radiation Oncology, Muscat, Oman
[3]Suez University Faculty of Medicine, Department of Clinical Oncology and Nuclear Medicine, Suez, Egypt
[4]International Atomic Energy Agency, Department of Nuclear Sciences and Applications, Division of Human Health, Vienna, Austria

Abstract

Objectives: The management of locally advanced esophageal cancer (EC) has evolved considerably, with neoadjuvant chemoradiotherapy (nCRT) followed by surgery remaining the standard of care for eligible patients, and definitive chemoradiotherapy serving as an alternative for those who are medically unfit or who decline surgery. Real-world data from the Middle East are scarce. This study evaluates treatment outcomes at King Hussein Cancer Center (KHCC).

Methods: This single-center retrospective cohort study included all patients with locally advanced EC treated with curative-intent chemoradiotherapy at KHCC between 2014 and 2023. A broader institutional cohort was used to contextualize radiotherapy utilization over time. Survival endpoints-overall survival (OS), local control (LC), progression-free survival (PFS), and distant metastasis-free survival (DMFS)-were estimated by Kaplan-Meier analysis. Multivariable Cox regression with backward Akaike information criterion-based selection was performed.

Results: Fifty-four patients were analyzed. The median age was 59.5 years (range, 24-83), and 80.6% were male. Adenocarcinoma accounted for 74.1% and squamous cell carcinoma for 25.9% of cases. Tumors were predominantly located in the lower esophagus (79.6%). Surgery was performed in 24 patients (44.4%); of these, 95.8% achieved R0 resection and 16.7% attained a pathologic complete response. Median follow-up was 59.0 months. Median OS was 31.0 months; 12-, 24-, and 48-month OS rates were 84.8%, 66.2%, and 36.5%, respectively. The 48-month LC, PFS, and DMFS rates were 67.2%, 29.5%, and 28.5%, respectively. On multivariable analysis, surgery was significantly associated with improved LC [hazard ratio (HR) 0.18, 95% confidence interval (CI) 0.04-0.83, p=0.03] and OS (HR 0.37, 95% CI 0.16-0.89, p=0.03). At the institutional level, radiotherapy utilization increased over time (OR per year 1.16, p=0.062).

Conclusion: In this real-world cohort, surgical resection following nCRT was associated with improved LC and OS. Definitive CRT provided meaningful disease control in carefully selected patients, particularly those unfit for surgery. These findings support multidisciplinary decision-making and warrant prospective validation to refine selection criteria for non-operative strategies.

Keywords: Esophageal cancer, chemoradiotherapy, real-world outcomes, trimodality therapy, definitive CRT, Jordan

Introduction

Esophageal cancer (EC) is considered a major global health problem, it is the seventh most prevalent cancer worldwide and the sixth leading cause of cancer mortality, accounting for approximately 604.000 new cases and 544.000 deaths in 2020 (1). The two dominated histological subtypes-squamous cell carcinoma (SCC) and adenocarcinoma (AC)-differ in geographic distribution, risk factors, and response to treatment, with SCC predominating in developing regions and AC rising sharply in Western populations (2,3).

In Jordan, the Jordan Cancer Registry documented a steady increase in gastrointestinal malignancies between 2000 and 2013, driven by demographic growth, rising life expectancy,

Address for Correspondence: Jamal Khader, MD, King Hussein Cancer Center (KHCC), Department of Radiation Oncology, Amman, Jordan
E-mail: jkhader@khcc.jo **ORCID:** orcid.org/0000-0003-0915-2943
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and lifestyle risk factors including tobacco use, obesity, and gastroesophageal reflux disease (4,5). GLOBOCAN data estimate approximately 33 new EC cases per year in Jordan, with an age-standardized incidence rate of approximately 0.9 per 100.000 in males (6). Notably, a global survival analysis identified Jordan as having the highest age-standardized five-year relative survival among low- and middle-income countries for EC (2010-2014; 41.1%), likely reflecting concentrated specialized oncologic care at centers such as King Hussein Cancer Center (KHCC) (7).

The management of locally advanced EC has evolved substantially over the past two decades. The CROSS regimen with neoadjuvant chemoradiotherapy (nCRT) (carboplatin/paclitaxel given concurrently with 41.4 Gy in 23 fractions) followed by esophagectomy, indicating a great survival advantage over surgery alone [median overall survival (OS) 48.6 vs. 24.0 months] and established as a standard approach for resectable disease (8,9). More recently, the ESOPEC trial showed the superiority of perioperative fluorouracil, leucovorin, oxaliplatin, and docetaxel (FLOT) chemotherapy over nCRT for esophageal AC (10), while neo-AEGIS found no significant difference between CROSS and perioperative MAGIC/FLOT (11). Adjuvant nivolumab following nCRT and surgery was further established as standard of care for patients without pathologic complete response (pCR) in CheckMate 577 (12).

Parallel to these developments, definitive chemoradiotherapy (dCRT) has emerged as a curative-intent alternative for patients who are not medically fit for, or who decline, surgery. The ARTDECO trial established 50-50.4 Gy in 25-28 fractions as the standard dose without benefit from escalation (13), and organ-preservation strategies are being prospectively evaluated in the SANO and NEEDs trials, particularly for SCC (14,15). Given this evolving landscape, real-world outcome data from underrepresented regions are limited, and such data are needed to validate institutional practice and inform local treatment optimization.

Our study aims to assess the real-world outcomes of chemoradiotherapy, with or without surgical resection, in patients with locally advanced EC who were treated in a resource-limited setting.

Material and Methods

Study Design and Patient Selection

This was a single-center, retrospective cohort study conducted at KHCC.

We first identified all adult patients (aged 18 years or older) diagnosed with or initially evaluated for EC at KHCC between January 2014 and December 2023 using institutional registry data. This cohort was used to describe annual case volume and to assess the representativeness of the radiotherapy-treated population.

From this source population, we selected cases of locally advanced EC treated with curative-intent concurrent chemoradiotherapy, and they were included in the analytic cohort. Patients with incomplete medical records, insufficient treatment documentation, or no evaluable follow-up were excluded.

Using unique medical record numbers, Patients in the analytic cohort were linked to the institutional cohort to determine the proportion of EC patients who received radiotherapy each year. Temporal trends in radiotherapy cohort inclusion were assessed using univariable logistic regression, with cohort inclusion as the dependent variable and calendar year as a continuous independent variable. An exploratory multivariable model including age, sex, and histological subtype was attempted but not used for inference because it failed to converge owing to the small sample size and sparse data.

The King Hussein Cancer Center Institutional Review Board approved the study protocol (approval no: 24 KHCC 223, date: 17.11.2024) and waived informed consent because of the retrospective nature of the analysis.

Data Collection

Clinical information and treatment data were abstracted from the institution's electronic medical record system and the radiotherapy electronic record system. The data collected included patient demographics (age, performance status, sex), tumor characteristics (histological subtype, location, length, clinical T and N stages), treatment details (chemotherapy regimen, radiotherapy dose and fractionation, surgical details), and outcomes (pathologic response, patterns of failure, and survival).

Surgical Management

Surgical resection was offered to, and discussed with, all patients who had resectable, locally advanced EC as part of trimodality therapy in a multidisciplinary team (MDT) setting. Patients who were medically unfit due to significant comorbidities, poor performance status, or inadequate cardiopulmonary reserve and those who declined operative intervention after MDT counseling received dCRT as the primary curative strategy.

Systemic Therapy

Concurrent chemotherapy was administered with all radiotherapy regimens. The primary regimen at our institution consisted of weekly carboplatin (area under the curve 2) and paclitaxel (50 mg/m^2), used predominantly with neoadjuvant intent in both AC and SCC. Cisplatin (70-75 mg/m^2) combined with 5-fluorouracil (5-FU; 2.100-3.200 mg/m^2 over 96 hours) is used as an alternative, particularly for upper or cervical esophageal tumors. A folinic acid, fluorouracil, and oxaliplatin (FOLFOX)-based schedule (oxaliplatin 85 mg/m^2, leucovorin 400 mg/m^2, 5-FU 400 mg/m^2 bolus, then 2.400 mg/m^2 over 46 hours) was employed in patients with contraindications to taxanes or cisplatin.

Radiotherapy

All radiotherapy was planned and delivered per the KHCC Gastrointestinal Radiotherapy Guidelines (15). Volumetric arc therapy or intensity-modulated radiotherapy was the preferred technique; three-dimensional conformal radiotherapy was reserved for situations in which advanced planning was not applicable. Image-guided daily cone-beam computed tomography (CT) was standard. Contrast-enhanced planning CT was performed in the supine position, with both arms raised above the head. The gross tumor volume (GTV) encompassed the primary tumor and any radiologically or metabolically involved lymph nodes, and was delineated by integrating positron emission tomography-CT and endoscopic findings. A 3 cm cranio-caudal and 1 cm radial margin beyond the primary GTV was applied to the clinical target volume (CTV), with a 1 cm isotropic margin around the nodal GTV; the planning target volume was generated from the CTV using patient- and site-specific margins.

For neoadjuvant CRT, the standard dose was 41.4-50.4 Gy in 23-28 fractions (1.8 Gy/fraction, 5 days/week). For definitive CRT, 50-50.4 Gy in 25-28 fractions was prescribed, with an optional sequential boost to 60 Gy in 30 fractions in selected cases, when clinically indicated.

Endpoints

Time-to-event endpoints were calculated from the date of radiotherapy initiation. The primary endpoint was OS, defined as the interval from radiotherapy initiation to death from any cause or last documented follow-up. Secondary endpoints were: local control (LC), defined as the absence of locoregional failure within the radiation field; distant metastasis-free survival (DMFS), defined as the time to the first documented distant metastasis; and progression-free survival (PFS), defined as the time to any disease progression or death, whichever occurred first. Patterns of failure (locoregional, distant, or combined) were also described.

Statistical Analysis

Python (version 3.12.7) was used to conduct all the analyses. Descriptive statistics were used to summarize patient and treatment characteristics. Baseline characteristics between surgical and non-surgical groups were compared using appropriate non-parametric and categorical tests. The Kaplan-Meier method was used to estimate the survival endpoints, with survival rates estimated at 12, 24, and 48 months. The reverse Kaplan-Meier method was used to estimate follow-up duration. Univariable comparisons were performed using the log-rank test. Given the limited cohort size and number of events, multivariable Cox models were intentionally restricted to clinically relevant variables to reduce overfitting. Multivariable Cox proportional hazards regression models were constructed with radiotherapy dose, histological subtype, and surgical status as initial covariates; backward stepwise selection based on the Akaike information criterion (AIC) identified the most parsimonious models using the lifelines package. A p-value ≤0.05 was considered statistically significant.

Results

Institutional Case Volume and Radiotherapy Cohort Representation

Between 2014 and 2023, 162 patients with EC were identified at our institution. Annual case volume ranged from 9 patients in 2014 to a peak of 29 in 2019.

Overall, 54 patients (33.3%) were included in the radiotherapy cohort. The proportion of patients receiving radiotherapy varied over time: it increased from 11.1% in 2014 to 29.4% in 2023, with a peak of 37.9% in 2019 (Figure 1).

In univariable logistic regression analysis, calendar year was associated with a non-significant trend toward increased likelihood of inclusion in the radiotherapy cohort [odds ratio per year 1.16, 95% confidence interval (CI) 0.99-1.34, p=0.062].

The exploratory multivariable model was not interpretable due to non-convergence.

Patient and Tumor Characteristics

A total of 54 patients met the eligibility criteria and were included in the analysis; the median age was 59.5 years (range 24-83 years), and 80.6% were male. AC was the predominant histology (74.1%), with squamous cell carcinoma comprising

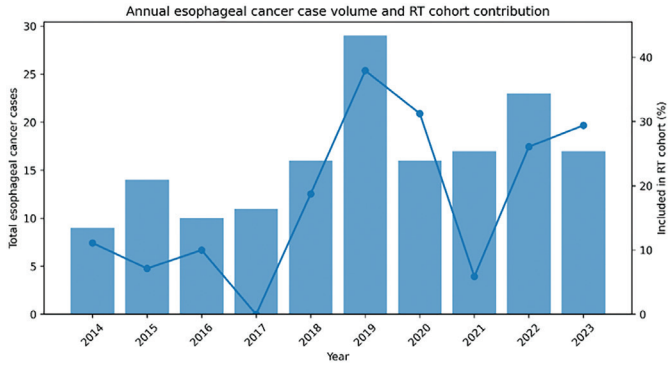


Figure 1. Annual institutional esophageal cancer case volume and radiotherapy (RT) cohort contribution. Bars represent the total number of esophageal cancer patients diagnosed or first encountered at the institution in each year from 2014 to 2023. The line represents the annual proportion of patients included in the radiotherapy cohort

the remaining 25.9%. The predominant tumor grade was grade 2 (55.6%), followed by grade 3 (42.6%) and grade 1 (1.9%). The median tumor length was 5.0 cm [interquartile range (IQR) 3.0-6.0 cm]. Tumors were most commonly located in the lower esophagus (79.6%), followed by the middle (18.5%) and upper esophagus (1.9%).

Table 1 shows baseline characteristics stratified by surgical status. Patients who underwent surgery were significantly younger than those managed without surgery (median age, 50.0 vs. 63.5 years; p=0.001) and were more likely to have received neoadjuvant chemotherapy (95.8% vs. 73.3%; p=0.033) and had a higher median number of chemotherapy cycles (5.0 vs. 4.0; p=0.028). Histology also differed numerically: AC was more common in the surgical cohort (87.5% vs. 63.3%), whereas squamous cell carcinoma was more common in the non-surgical cohort (36.7% vs. 12.5%); however, this finding was not statistically significant (p=0.062). Radiotherapy dose and fractionation were numerically higher in the non-surgical cohort, consistent with definitive treatment intent; however, these differences were not statistically significant. Clinical nodal status, M stage, performance status, tumor location, and grade ≥2 toxicity were not significantly different between groups.

Treatment Details

All 54 patients received concurrent chemoradiotherapy, administered either as nCRT preceding surgery or as dCRT. Neoadjuvant CRT regimens included carboplatin plus paclitaxel delivered at 41.4-50.4 Gy and cisplatin plus 5-FU delivered at 50-50.4 Gy. Definitive CRT regimens comprised cisplatin plus 5-FU (50.4 Gy) or FOLFOX (50.4 Gy). Surgical resection was performed in 24 patients (44.4%), while 30 patients (55.6%) received dCRT without surgery. Among surgical patients, 95.8% achieved R0 resection, and pCR was documented in 16.7%.

Survival Outcomes

The median follow-up for the entire cohort was 59.0 months (IQR, 19.0-70.0 months). The median OS was 31.0 months (IQR 19.0-70.0 months),with 12-, 24-, and 48-month OS rates of 84.8%, 66.2%, and 36.5%, respectively. The median PFS was 17.0 months (IQR 11.0-70.0 months); 12-, 24-, and 48-month PFS rates were 69.0%, 40.9%, and 29.5%. The median DMFS was 20.0 months (IQR 14.0-70.0 months), with 12-, 24-, and 48-month rates of 79.2%, 46.9%, and 28.5%, respectively. LC was not reached; 12-, 24-, and 48-month LC probabilities were 79.0%, 73.3%, and 67.2% (Figure 2).

Univariable Analyses

In univariable log-rank testing, surgical resection was significantly associated with improved LC (p=0.0134, Figure 3). Histological subtype and pCR status did not demonstrate a significant relationship with LC (p=0.237 and p=0.502, respectively), as displayed in Supplementary Figure 1. For DMFS, PFS, and OS, no statistically significant associations were identified, although surgery and OS approached statistical significance (p=0.055).

Multivariable Cox Regression

Multivariable Cox regression with backward stepwise AIC-based selection was performed for each endpoint, with radiotherapy dose, histological subtype (SCC vs. AC), and surgical status included as initial covariates. Results are depicted in Table 2. For LC, the final model retained surgical status as the sole predictor, with surgery associated with a markedly lower hazard of locoregional failure [hazard ratio (HR) 0.18, 95% CI 0.04-0.83, p=0.03]. For DMFS, radiotherapy dose was the only retained variable, but it did not reach significance (HR 0.96, 95% CI 0.89-1.03, p=0.28). Similarly, for PFS, radiotherapy dose was retained but was not statistically significant (HR 0.98, 95% CI 0.91-1.05, p=0.56). For OS, the final model included both radiotherapy dose and surgery; the dose was not significant (HR 0.93, 95% CI 0.85-1.02, p=0.12), while surgery remained an independent predictor (HR 0.37, 95% CI 0.16-0.89, p=0.03).

Given the observed age imbalance by surgical status, an unplanned sensitivity analysis using a Cox model including both surgical status and age was performed. As shown in Supplementary Table 1, surgical resection was independently associated with improved OS (HR 0.37, 95% CI 0.14-0.97, p=0.044), whereas age was not significantly associated with outcome (HR 0.99 per year, 95% CI 0.96-1.02, p=0.41).

Discussion

In this retrospective study of 54 cases of locally advanced EC treated at KHCC, surgical resection following nCRT was associated with improved LC and OS. These findings are consistent with the CROSS trial, which demonstrated the superiority of trimodality therapy over surgery alone (8,9), and reinforce the role of esophagectomy as an integral component of curative-intent treatment for eligible patients.

However, findings must be interpreted cautiously, given that surgical patients were younger and more frequently received neoadjuvant chemotherapy, which underscores the likelihood of treatment-selection bias. Importantly, surgical resection remained associated with improved OS in

Table 1. Baseline patient, tumor, and treatment characteristics stratified by surgical resection status

Characteristic	Overall, n=54	No surgery, n=30	Surgery, n=24	p-value
Demographics and treatment variables				
Age at diagnosis, median (IQR), years	59.5 (47.2-69.8)	63.5 (52.2-75.0)	50.0 (42.0-60.2)	0.001
Tumor length, median (IQR), cm	5.0 (3.0-6.0)	5.0 (3.0-6.0)	4.0 (3.2-6.0)	0.699
Neoadjuvant chemotherapy cycles, median (IQR)	4.0 (4.0-5.0)	4.0 (0.8-5.0)	5.0 (4.0-5.0)	0.028
Radiotherapy dose, median (IQR), Gy	41.4 (41.4-50.4)	47.5 (41.4-50.4)	41.4 (41.4-50.0)	0.114
Radiotherapy fractions, median (IQR)	23.0 (23.0-28.0)	25.0 (23.0-28.0)	23.0 (23.0-25.0)	0.087
Sex				0.157
Female	10 (18.5%)	8 (26.7%)	2 (8.3%)	
Male	44 (81.5%)	22 (73.3%)	22 (91.7%)	
Histology				0.062
Adenocarcinoma	40 (74.1%)	19 (63.3%)	21 (87.5%)	
Squamous cell carcinoma	14 (25.9%)	11 (36.7%)	3 (12.5%)	
Tumor grade				0.455
Grade 1	1 (1.9%)	0 (0.0%)	1 (4.2%)	
Grade 2	30 (55.6%)	16 (53.3%)	14 (58.3%)	
Grade 3	23 (42.6%)	14 (46.7%)	9 (37.5%)	
Tumor location				0.371
Lower	43 (79.6%)	22 (73.3%)	21 (87.5%)	
Middle	10 (18.5%)	7 (23.3%)	3 (12.5%)	
Upper	1 (1.9%)	1 (3.3%)	0 (0.0%)	
Clinical N stage				0.261
N+	33 (63.5%)	17 (56.7%)	16 (72.7%)	
N0	19 (36.5%)	13 (43.3%)	6 (27.3%)	
M stage				1.000
M0	52 (96.3%)	29 (96.7%)	23 (95.8%)	
M1	2 (3.7%)	1 (3.3%)	1 (4.2%)	
Performance status				0.497
0-1	52 (96.3%)	28 (93.3%)	24 (100.0%)	
2	2 (3.7%)	2 (6.7%)	0 (0.0%)	
Neoadjuvant chemotherapy				0.033
No	9 (16.7%)	8 (26.7%)	1 (4.2%)	
Yes	45 (83.3%)	22 (73.3%)	23 (95.8%)	
Grade ≥2 toxicity				1.000
No	36 (66.7%)	20 (66.7%)	16 (66.7%)	
Yes	18 (33.3%)	10 (33.3%)	8 (33.3%)	

Values are presented as number (%) unless otherwise specified. Continuous variables are summarized as median and interquartile range (IQR). Percentages were calculated using available non-missing data for each variable. Comparisons between surgical and non-surgical cohorts were performed using the Mann-Whitney U test for continuous variables and Fisher's exact test or chi-square test for categorical variables, as appropriate. Clinical N stage percentages were calculated among patients with available nodal staging data

Gy: Gray, N+: Node-positive disease, N0: Node-negative disease

a sensitivity analysis adjusting for age, suggesting that the observed survival benefit was not solely explained by age differences between treatment groups.

Histological subtype was not significantly associated with outcomes. The absence of a radiotherapy dose-response relationship may reflect the relatively narrow dose range across the cohort-all within established therapeutic windows-suggesting that further dose variation within standard ranges does not meaningfully alter outcomes (16). The lack of a histology effect contrasts with larger cohorts reporting higher CRT responsiveness in SCC (17), and may be explained by the small sample size and preponderance of AC (74.1%) in this cohort, reflecting lower esophageal predominance

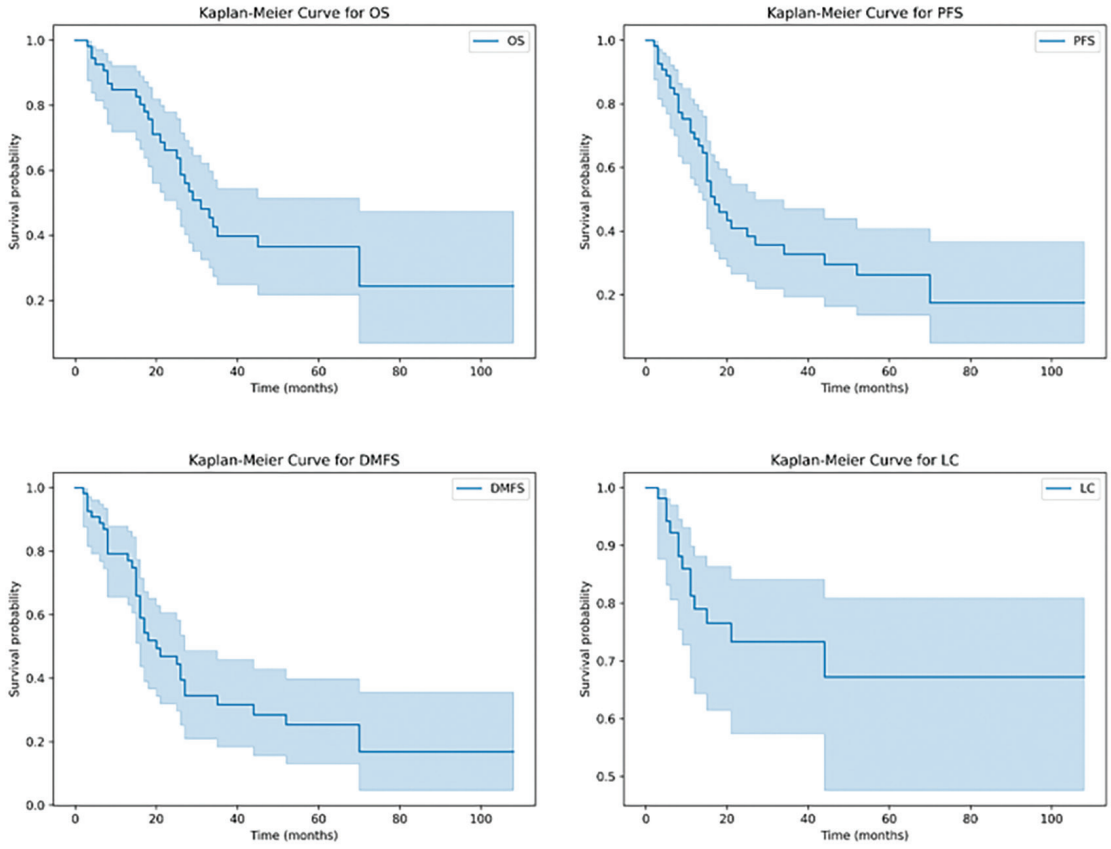


Figure 2. Kaplan-Meier curves for OS, PFS, DMFS, and LC. Shaded areas represent 95% confidence intervals; time is measured from radiotherapy initiation

OS: Overall survival, PFS: Progression-free survival, DMFS: Distant metastasis-free survival, LC: Local control

Table 2. Multivariable Cox proportional hazards models for survival outcomes

Endpoint	Final selected covariate	HR	95% CI	p-value	Events/n	Concordance	Partial AIC
Local control	Surgery, yes vs. no	0.18	0.04-0.83	0.03	13/54	0.69	88.91
Distant metastasis-free survival	Radiotherapy dose, per 1 Gy increase	0.96	0.89-1.03	0.28	34/54	0.52	223.41
Progression-free survival	Radiotherapy dose, per 1 Gy increase	0.98	0.91-1.05	0.56	34/54	0.48	226.18
Overall survival	Radiotherapy dose, per 1 Gy increase	0.93	0.85-1.02	0.12	28/54	0.64	183.62
Overall survival	Surgery, yes vs. no	0.37	0.16-0.89	0.03	28/54	0.64	183.62

Multivariable Cox proportional hazards regression models were constructed separately for local control, distant metastasis-free survival, progression-free survival, and overall survival. Initial candidate covariates included radiotherapy dose, histology, and surgery. Final models were selected using backward stepwise selection based on the Akaike information criterion (AIC). Hazard ratios (HRs) below 1 indicate a lower hazard of the event. For radiotherapy dose, the HR reflects the change in hazard per 1 Gy increase. For surgery, the reference category was no surgery

CI: Confidence interval, Gy: Gray

characteristic of the Middle East and North Africa (MENA) region.

Although pCR was achieved in 16.7% of surgical patients, this did not translate into a statistically significant survival improvement, likely due to limited statistical power rather than a true biological absence of effect; the prognostic value of pCR is well-established in larger series (18,19). The rate observed is lower than the 29% for AC and 49% for SCC in the original CROSS trial (8), which may reflect differences in patient selection, chemotherapy utilization, and tumor biology in this real-world setting.

In the non-operative cohort, 30 patients (55.6%) received dCRT without surgery. The 48-month LC rate of 67.2% was relatively favorable, suggesting that dCRT can achieve durable locoregional control in a meaningful proportion of patients. The ARTDECO and PRODIGE-5/ACCORD-17 trials have established 50-50.4 Gy concurrent with carboplatin/paclitaxel or FOLFOX as effective dCRT regimens (13,20), and our institutional outcomes appear broadly consistent with this evidence. Emerging organ-preservation data from the SANO trial demonstrate that in carefully selected patients who achieve a clinical complete response, esophagectomy may be safely deferred, with salvage surgery reserved for recurrence (14), an approach further supported by our findings within a structured MDT framework.

The most significant challenge in this cohort was distant failure, as reflected by DMFS declining to 28.5% at 48 months. The high rate of distant failure highlights systemic disease as the dominant mode of relapse, suggesting that improvements in systemic therapy, rather than locoregional intensification, are most likely to improve long-term outcomes (21). Adjuvant nivolumab (CheckMate 577) (12) and perioperative FLOT (ESOPEC) (10) represent important advances that may improve outcomes in future cohorts at KHCC.

This study provides real-world data from a Middle Eastern tertiary cancer center, contributing to the limited literature on EC outcomes from the MENA region. Institutional outcomes at KHCC are broadly comparable to published data from high-income Western centers, which supports the quality of care delivered within the multidisciplinary framework.

An observation from this study is the increasing

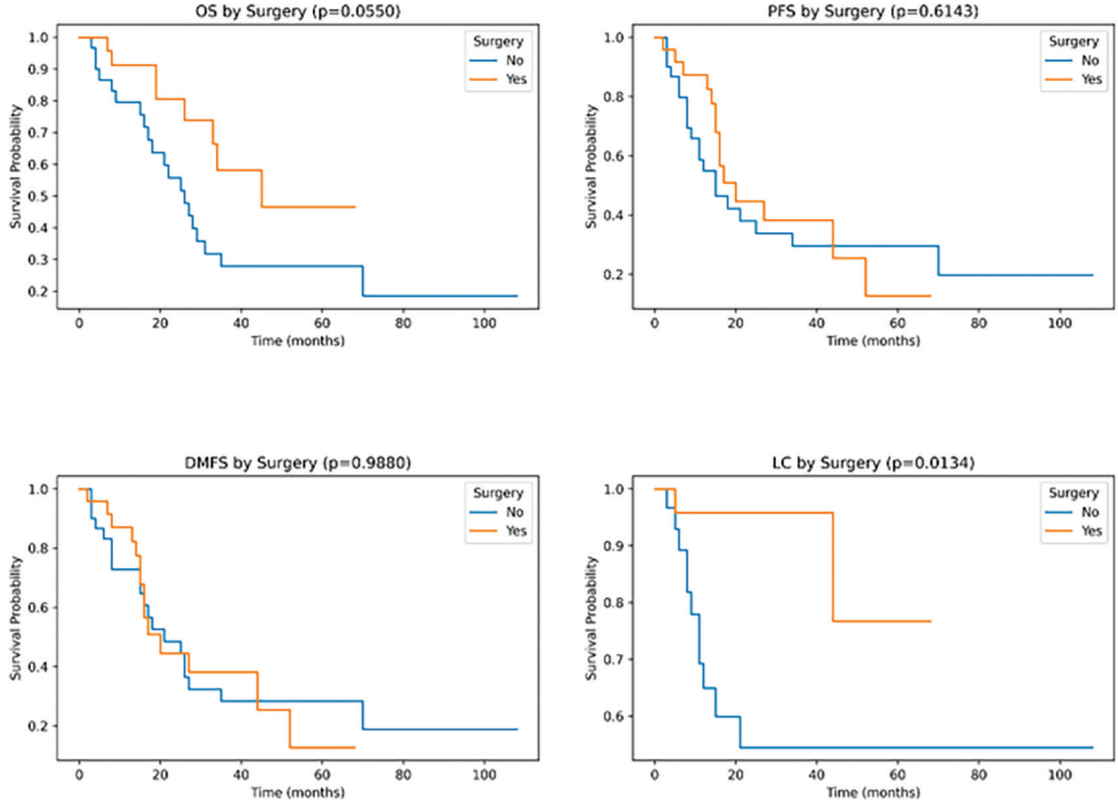


Figure 3. Kaplan-Meier curves stratified by surgery

Surgery was associated with improved local control (p=0.0134) and a trend toward improved OS (p=0.055), with no significant differences in PFS or DMFS

OS: Overall survival, PFS: Progression-free survival, DMFS: Distant metastasis-free survival, LC: Local control

representation of radiotherapy-treated patients, manifested as a non-significant trend toward higher inclusion in the radiotherapy cohort across calendar years. Although not statistically significant, this pattern likely reflects evolving multidisciplinary practice, improved access to advanced radiotherapy techniques, and greater acceptance of organ-preservation strategies. Such temporal shifts are consistent with broader global trends toward individualized treatment selection and may partially explain the heterogeneity observed in real-world cohorts.

Study Limitations

Several limitations merit emphasis. The retrospective design and limited sample size reduce statistical power and generalizability, and selection bias cannot be excluded because surgical patients likely had better performance status and more favorable tumor characteristics than those managed with dCRT. Treatment regimens were heterogeneous, reflecting the evolving landscape of clinical practice over the ten-year study period. Prospective, adequately powered studies with standardized protocols and systematic toxicity reporting are needed to validate these findings and refine patient selection for operative and non-operative strategies. Additionally, temporal changes in referral patterns and treatment selection may have influenced cohort composition over the study period.

Conclusion

Among patients with locally advanced EC treated in a real-world setting, surgical resection following nCRT was independently associated with significantly improved LC and OS. dCRT without surgery offered a viable treatment strategy in carefully selected patients, particularly those who were medically unfit or who declined operative management. The predominant mode of treatment failure was distant metastasis, highlighting the urgent need for more effective systemic therapies. Future studies incorporating radiomics, molecular profiling, and response-adapted strategies may help refine selection for organ-preservation approaches.

Ethics

Ethics Committee Approval: The King Hussein Cancer Center Institutional Review Board approved the study protocol (approval no: 24 KHCC 223, date: 17.11.2024).

Informed Consent: Waived informed consent because of the retrospective nature of the analysis.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ab.A., F.A., J.K., Concept: An.A., Ab.A., Design: An.A., Ab.A., Data Collection or Processing: An.A., M.Q., O.K., Analysis or Interpretation: Ab.A., Literature Search: An.A., M.Q., S.S., O.K., F.A., S.M., A.E., I.M., J.K., Writing: An.A., Ab.A., M.Q., S.S., O.K., F.A., S.M., A.E., I.M., J.K.

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

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Supplementary Figure: https://d2v96fxpocvxx.cloudfront.net/8cc23056-a98a-4545-ab3f-e10be6b0f046/content-images/13cd7f9b-c632-40ac-b6b1-44b3bf013aa6.pdf

Supplementary Table: https://d2v96fxpocvxx.cloudfront.net/8cc23056-a98a-4545-ab3f-e10be6b0f046/content-images/4f744186-02a4-4795-934e-1b2662e6a47f.pdf

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Evaluation Questions

Based on the manuscript: "Real-world Outcomes of Chemoradiotherapy with or Without Surgery in Locally Advanced Esophageal Cancer: A Retrospective Analysis"

1. Which trial demonstrated superiority of perioperative FLOT over CROSS in esophageal adenocarcinoma?

A. CheckMate 577

B. Neo-AEGIS

C. ESOPEC

D. ARTDECO

E. SANO

2. What is the standard radiotherapy dose for definitive CRT in esophageal cancer?

A. 30 Gy

B. 41.4 Gy

C. 45 Gy

D. 50-50.4 Gy

E. 60-66 Gy

3. Which finding supports adjuvant nivolumab after nCRT and R0 esophagectomy?

A. Pathologic complete response

B. Residual pathologic disease

C. PD-L1 positivity alone

D. HER2 amplification

E. MSI-high status alone

4. Which strategy was evaluated in SANO for patients with clinical complete response after nCRT?

A. Adjuvant chemotherapy

B. Radiotherapy boost

C. Active surveillance with salvage surgery when indicated

D. Maintenance immunotherapy

E. Immediate surgery for all patients

5. Which histological subtype generally shows greater sensitivity to CRT in esophageal cancer?

A. Adenocarcinoma

B. Squamous cell carcinoma

C. Neuroendocrine carcinoma

D. Small cell carcinoma

E. Sarcomatoid carcinoma

Correct Answers: 1C, 2D, 3B, 4C, 5B