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Esophageal cancer surgery 5-year survival rate and predictors of operative mortality—a single-center analysis

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Ethics Committee Approval
All procedures were carried out in accordance with the requirements set forth by the institutional ethics committee, as well as those outlined in the 1964 Declaration of Helsinki and its subsequent amendments. Before each procedure, individual, free, informed, and clarified consent was obtained from each patient.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Esophagectomy remains the primary curative option for esophageal cancer; however, survival outcomes vary based on treatment strategies, tumor staging, and surgical techniques. This study evaluated the survival rates of patients undergoing esophagectomy and assessed factors influencing postoperative prognosis.

Methods: A retrospective observational study was conducted of 75 patients undergoing esophagectomy between 2017 and 2024 at a single tertiary center. Fifty-nine patients had esophageal and gastroesophageal junction malignancies and were non-randomly allocated to one of three treatment arms: primary surgery, neoadjuvant chemoradiotherapy (CROSS) followed by surgery, and perioperative chemotherapy (FLOT) followed by surgery. Survival analysis was performed using Kaplan-Meier estimates, and prognostic factors were assessed using multivariate statistical tests.

Results: The overall 5-year survival rate was 32%. Patients in the FLOT group had a higher survival rate than patients in the CROSS and primary surgery groups. However, the difference was not statistically significant (P=0.121). Pathological staging significantly impacted survival, with stage I patients having a 52% 5-year survival rate. McKeown esophagectomy was associated with the lowest survival rate (11%); transhiatal esophagectomy exhibited the highest anastomotic leak rate (50%). The Surgical Apgar Score (SAS) was a strong predictor of perioperative risk (AUC=0.94, P<0.001).

Conclusion*:* Postoperative pathological staging remains the strongest predictor of survival in esophageal cancer surgery. While neoadjuvancy showed promising trends, additional studies are necessary to optimize patient selection and evaluate the role of active surveillance strategies in long-term outcomes.

Keywords: esophagus, esophageal neoplasms, esophagectomy, survival rate, neoadjuvant therapy

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Introduction

Esophageal cancer, the eighth most common malignancy, is one of the most aggressive neoplasms of the digestive system; it has a generally poor prognosis and high mortality rates worldwide [1,2]. Surgical resection remains the primary curative approach, particularly in early-stage disease, although it is widely accepted that its combination with preoperative chemoradiation greatly improves outcomes [3].

On the other hand, despite true gastroesophageal junction (GEJ) adenocarcinoma (ADC) (Siewert type II) being a rare, distinct entity that is difficult to treat, there has been a growing trend in favor of perioperative chemotherapy instead of chemoradiation [4,5]. In either case, from a surgical standpoint GEJ cancer surgery implies an esophagectomy. Practitioners are increasingly adopting a more extensive esophageal resection approach providing a margin of safety and lymphadenectomy improvements [4,5].

The survival rate of patients undergoing esophagectomy varies significantly depending on multiple factors, including tumor stage, histological subtype, surgical technique, and perioperative management [6].

Despite advances in surgical techniques and perioperative care, esophagectomy is associated with significant morbidity and mortality. Postoperative complications, including anastomotic leaks, infections, and pulmonary complications, can severely impact short- and long-term survival [7,8]. The implementation of minimally invasive surgical techniques has demonstrated some benefits in terms of reducing postoperative complications. However, the impact of such techniques on operative mortality and long-term survival remains a subject of ongoing research [9,10].

Several studies have analyzed the survival rates of esophageal cancer patients post-surgery, with 5-year survival rates ranging from 15–50% [11,12]. Most studies cite sub-25% survival rates that depend on tumor characteristics and treatment protocols [13,14]. Understanding the factors that influence survival outcomes can provide valuable insights into optimizing patient selection, improving surgical strategies, and enhancing perioperative management to maximize survival benefits.

One valuable tool for assessing perioperative risk and predicting postoperative outcomes is the Surgical Apgar Score (SAS). The SAS, originally developed by Gawande et al. [15], is based on intraoperative parameters such as estimated blood loss, lowest mean arterial pressure, and lowest heart rate. Studies have shown that lower SAS scores correlate with higher rates of postoperative complications and mortality across various surgical disciplines, including gastrointestinal surgery [16]. Recent research suggests that SAS may be a useful predictor of short- and long-term survival following esophagectomy, allowing for better risk stratification and postoperative management [17].

In addition to surgical interventions, recent trials have explored non-surgical management approaches for esophageal cancer. The Surgery As Needed for Oesophageal cancer (SANO) trial introduced a “watch-and-wait” strategy for patients with a complete clinical response following neoadjuvant chemoradiotherapy (NCRT), thereby avoiding immediate surgery unless tumor recurrence is detected [18]. The trial findings suggested that a non-operative approach may lead to similar survival outcomes while reducing surgical morbidity, challenging the traditional paradigm of mandatory esophagectomy after NCRT [19]. However, long-term follow-up is necessary to confirm the longitudinal nature of this strategy and its impact on overall survival and quality of life [20,21].

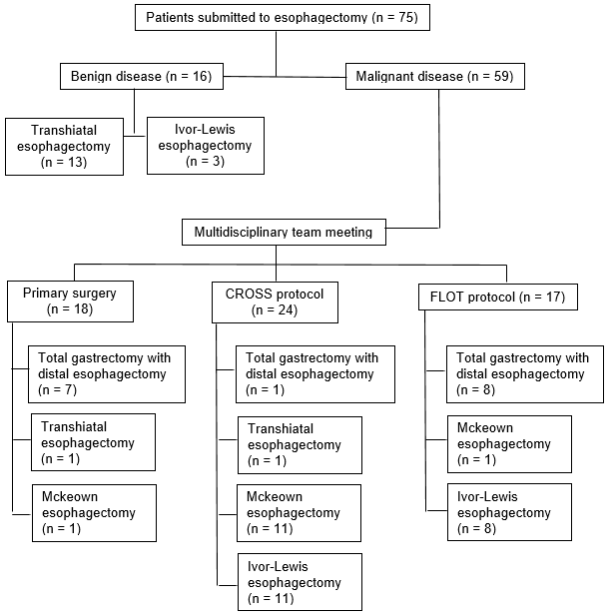
This study analyzes the survival rates of patients who have undergone surgical treatment for esophageal and GEJ cancer at a single tertiary center, considering various prognostic factors such as staging, procedure choice, and patient characteristics that may influence overall survival. By examining clinical and pathological variables, including perioperative risk scores such as SAS, this research seeks to contribute to improved patient management and treatment decision-making.

Materials and methods

Study design

This retrospective observational study focused on 75 patients who underwent esophagectomy between 2017 and 2024. Patient allocation was non-random and dictated by several clinical factors. Sixteen of the patients underwent transhiatal (n=13) or Ivor-Lewis esophagectomy (n=3) due to benign disease, such as end-stage achalasia, severe caustic injury with non-healing strictures, non-responsive esophageal strictures and benign neoplasms, and were therefore excluded from the oncological sample analysis. All oncological patients (n=59) were evaluated at a tertiary center multidisciplinary meeting with General Surgeons, Gastroenterologists, Medical and Radiation Oncologists, Pathologists and Radiologists, in which each case was individually discussed and a treatment strategy was selected according to tumor location, histological subtype, clinical staging, patient comorbidities, and performance status, among other factors. That processes therefore introduced a clinically mandated selection bias. These patients were selected for primary surgery (n=18), neoadjuvant chemoradiotherapy followed by surgery according to the CROSS protocol6 (n=24), or perioperative chemotherapy followed by surgery according to the FLOT protocol5 (n=17) [figure 1].

Figure 1. Patients included in the study



CROSS: Chemoradiotherapy for Oesophageal cancer followed by Surgery Study protocol, FLOT: Fluorouracil, Leucovorin, Oxaliplatin and Docetaxel protocol

This study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure transparency, completeness, and accuracy in reporting observational research.

Outcomes

Primary goals encompassed calculation and plotting of 5-year survival curves for the overall sample as well as for the oncological group. Survival was then compared between treatment strategy allocation arms, procedure-related allocation and according to postoperative staging.

Secondary goals included analysis of predicted versus observed mortality as well as complications, namely the anastomotic leak rate.

Statistical analysis

Data analysis was conducted using SPSS software version 26 (IBM Corp, Armonk, NY, USA). We applied the Shapiro-Wilk test to all of the variables to assess their normality. Nominal variables were expressed as absolute values and percentages and compared using the Pearson's chi-squared test with the post-hoc correction according to Bonferroni. Numerical variables were expressed as means ± standard deviation, if normally distributed, and subsequently compared with recourse to analysis of variance (ANOVA) and Tukey's post-hoc testing. Numerical data found to be non-parametric were expressed as medians (minimum – maximum) and compared using the Kruskal-Wallis test and Dunn's post-hoc correction.

Survival analysis was performed using Kaplan-Meier estimates, complemented by survival curve comparisons using the log-rank (Mantel-Cox) test to determine the presence of statistically significant differences.

Expected-versus-observed morbidity and mortality was assessed by plotting the Receiver Operating Characteristics (ROC) curves and calculating the Area Under the Curve (AUC) to determine sensitivity cut-off scores.

A *P*-value less than 0.05 was considered to indicate statistical significance.

Results

The 59 patients with esophageal malignant disease included in the study between 2017 and 2024 were assigned non-randomly to one of three treatment strategies [table 1]. However, the allocation differences were not statistically significant (X2 (2, n=59) = 2.169), *P*=0.338): 18 patients (30.5%) were directed being to primary surgery, 24 patients (40.7%) were directed to pre-operative chemoradiotherapy according to the CROSS protocol followed by surgery, and 17 patients (28.8%) were directed to peri-operative chemotherapy with the FLOT protocol followed by surgery.

The gender pool was asymmetric; however, this distribution remained homogenous between the treatment arms (*P*=0.085) [table 1].

Age at treatment was significantly different among the treatment groups (F (2, 56) = 5.442), *P*=0.007); post-hoc testing revealed that the patients in the primary surgery group were significantly older than the patients allocated to CROSS protocol.

Due to the treatment allocation being clinically oriented, the distribution was found to be significantly different between the study's groups (X2 (4, n=59) = 32.614), *P*<0.001); FLOT treatment was primarily chosen for GEJ ADC (n=16; 53.3%), and the CROSS treatment was primarily chosen for esophageal Squamous Cell Carcinoma (SCC) (n=14; 82.4%). Tumor location followed suit and exhibited a similar distribution pattern [table 1].

No significant differences in postoperative pathological staging (American Joint Committee on Cancer (AJCC) 8th edition) distributions were noted among the treatment arms (X2 (8, n=58) = 8.172, *P*=0.417) [table 1]. However, of the eight patients observed to have pathological complete response (13.8%), seven were in the CROSS group, and all of them were being treated for esophageal SCC (*P*=0.021).

The median follow-up duration was 13 months (range: 0–91 months); follow-up duration was similar for all of the treatment arms (H (2, n=59) = 4.128, *P*=0.127). All cause-mortality within the follow-up period was 54.2% (n=32) overall and 66.7% (n=12) for the primary surgery group; it was 58.3% (n=14) for the CROSS study arm and 35.3% (n=6) for the FLOT group (X2 (4, n=59 = 3.740, *P*=0.154) [table 1].

Mortality was plotted against follow-up time to obtain a survival function according to Kaplan-Meier; we recovered a median survival time of 20.0 months (95% CI 11.889; 28.111) and a 32% overall survival rate at 5 years [figure 2A]. Survival functions were also plotted for the treatment arms [figure 2B]; we did not find any significant differences among the groups according to the log-rank (Mantel-Cox) test (*P*=0.121). The primary surgery patients had a median survival duration of 19.0 months (95% CI 1.913; 36.087) and a 5-year survival rate of 23.5%. We found that 58% of the FLOT patients were alive 60 months after the procedure. The median survival duration for the CROSS group was 20.0 months (95% CI 11.294; 28.706); the survival rate at 60 months was 19.5%.

Figure 2A: Kaplan-Meier survival curve for the overall oncological patient sample

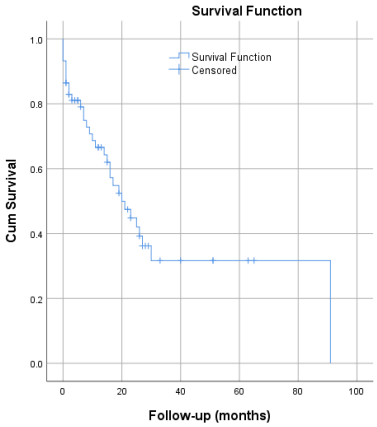


Figure 2B: Kaplan-Meier survival function based on treatment strategy allocation

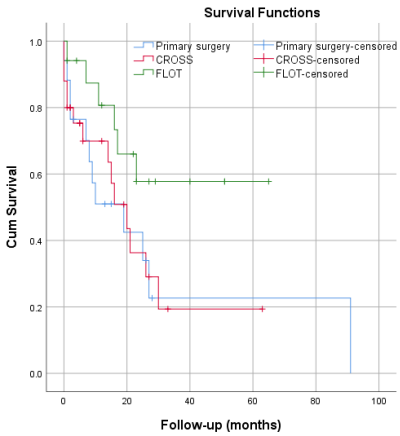


Table 1: Oncological sample characteristics

	Total sample	Primary surgery	CROSS	FLOT	*P*-value
N	59 (100%)	18 (30.5%)	24 (40.7%)	17 (28.8%)	0.338
Male	50 (84.7%)	15 (83.3%)	21 (87.5%)	14 (82.35%)	
Female	9 (15.3%)	3 (16.7%)	3 (12.5%)	3 (17.65%)	0.085
Age (years)	64 ±9.8	68.9 ±10.7	59.6 ±6.2	65 ±10.8	0.007
Histology					
Esophageal ADC	12 (20.3%)	3 (16.7%)	8 (33.3%)	1 (5.9%)	
GEJ ADC	30 (50.8%)	12 (66.6%)	2 (8.33%)	16 (94.1%)	<0.001
Esophageal SCC	17 (28.8%)	3 (16.7%)	14 (58.33%)	0	
Location					
Upper/Middle third	8 (13.5%)	0	8 (33.3%)	0	
Lower third	22 (37.3%)	6 (33.3%)	16 (66.7%)	0	<0.001
GEJ	29 (49.2%)	12 (66.7%)	0	17 (100%)	
Post-op staging					
I	18 (31.0%)	8 (44.5%)	5 (20.8%)	5 (29.4%)	
II	16 (27.6%)	4 (22.2%)	7 (29.2%)	6 (35.3%)	
III	14 (24.1%)	4 (22.2%)	5 (20.8%)	5 (29.4%)	0.417
IV	2 (3.4%)	2 (11.1%)	0	0	
Complete response	8 (13.8%)	0	7 (29.2%)	1 (5.9%)	0.021
Procedure					
TGDE	19 (32.2%)	10 (55.6%)	1 (4.2%)	8 (47.05%)	
TE	8 (13.6%)	7 (38.9%)	1 (4.2%)	0	
Mckeown	13 (22.0%)	1 (5.5%)	11 (45.8%)	1 (5.9%)	<0.001
Ivor-Lewis	19 (32.2%)	0	11 (45.8%)	8 (47.05%)	
Follow-up (months)	13 (0-91)	9.5 (0-91)	9 (0-63)	22 (1-65)	0.127
All-cause mortality	32 (54.2%)	12 (66.7%)	14 (58.3%)	6 (35.3%)	0.154

ADC: Adenocarcinoma, GEJ: Gastroesophageal Junction, SCC: Squamous Cell Carcinoma, TGDE: Total gastrectomy with distal esophagectomy, TE: Transhiatal esophagectomy

Table 2: Oncological sample procedure-related metrics

	TGDE	TE	Ivor-Lewis	Mckeown	*P*-value
(n=59)	19 (32.2%)	8 (13.6%)	19 (32.2%)	13 (22.0%)	
Location					
Upper/Middle third	0	0	2 (10.5%)	6 (46.2%)	
Lower third	1 (5.3%)	6 (75%)	9 (47.4%)	6 (46.2%)	<0.001
GEJ	18 (94.7%)	2 (25%)	8 (42.1%)	1 (7.6%)	
Lymphadenectomy	23.5 (15-50)	23 (3-33)	23 (7-53)	26 (7-54)	0.309
Intervention (min)	256 (152-454)	201 (152-329)	289 (238-401)	322 (285-429)	0.001
Hospital stay (days)	9 (3-24)	25 (10-56)	14 (8-87)	17 (4-62)	0.005
Follow-up (months)	15 (0-65)	9 (2-91)	11 (1-40)	16 (0-63)	0.938
Surgical Apgar Score	7 (4-9)	7 (4-8)	7 (4-9)	8 (5-9)	0.110
Anastomotic leak *(n=13)*	1 (5.3%)	4 (50%)	6 (31.6%)	2 (15.4%)	0.037
30-day mortality *(n=8)*	3 (15.8%)	0	1 (5.3%)	4 (30.8%)	0.125
All-cause mortality *(n=32)*	10 (52.6%)	5 (62.5%)	7 (36.8%)	10 (76.9%)	0.154

GEJ: Gastroesophageal Junction, TGDE: Total Gastrectomy with Distal Esophagectomy, TE: Transhiatal Esophagectomy

It is recognized that cancer staging is inversely related to survival, independent of treatment strategy [1]. That observation stands true for our study sample (P=0.02); we noted a cumulative 5-year survival rate of 52% for stage I patients (median: 51.0 months; 95% CI 30.964; 72.946) and a cumulative 5-year survival rate of 25% for stage II patients (at 52 months of follow-up). All stage III and IV patients had died by 30 and 2 months of follow-up, respectively. Individuals with a complete response after neoadjuvant therapy exhibited a survival rate of 75% (median cumulative survival not reached) [figure 3].

We also examined statistics pertaining to surgical procedure choice, which depended on tumor location and pre-operative characteristics; we noted significant differences in allocation (P<0.001) [table 2]. A median lymphadenectomy of 24 nodes (range: 3–54 nodes) was obtained; there were no significant differences among the four types of surgical procedures (H (3, n=59) = 3.593, P=0.309) [table 2].

We found that both Ivor-Lewis and McKeown esophagectomy were significantly lengthier procedures than transhiatal esophagectomy and total gastrectomy with distal esophagectomy (P=0.001); the latter was characterized by a shorter median hospital stay (9 days; range: 3–24 days) (H (3, n=59) = 13.018, P=0.005) [table 2].

The rate of complications, namely anastomotic leaks, was 50% (n=4) among patients who underwent transhiatal esophagectomy (n=8); it was 32% (n=6) among patients who underwent Ivor-Lewis esophagectomies. The latter rate is significantly higher than that of other procedures (X2 (3, n=59) = 8.467, P=0.037) [table 2]. Anastomotic dehiscence was treated endoscopically for the majority of cases; it was associated with a very high success rate and few re-operations. There was no mortality directly attributed to this cause.

Operative and all-cause mortality were identical among the procedures (P=0.125 and P=0.154, respectively). We produced Kaplan-Meier curves to compare the survival of the procedure-stratified groups [figure 4]. Patients who underwent total gastrectomy with distal esophagectomy had a 30% survival rate at the 5-year mark. Patients in the transhiatal esophagectomy arm exhibited a survival rate of 44% at 60 months; patients in the Ivor-Lewis group exhibited a survival rate of 48% at 40 months. The McKeown esophagectomy patients fared the worst; only 11% were alive after five years. However, the test of equality of survival distribution (i.e., the Mantel-Cox log rank) revealed no overall difference in survival rate (P=0.544).

We obtained SAS data for all patients (median score: 7; range: 4–9). We plotted those data against observed operative, 30-day mortality (n=8, which was found to be non-significantly different among the surgical procedures, P=0.125). The resultant ROC curve revealed an AUC of 94% (95% CI 0.887,1.0; P<0.001) [figure 5].

Figure 3: Kaplan-Meier survival function based on postoperative pathological staging

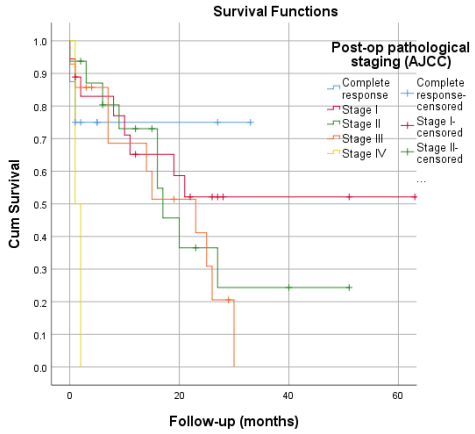


Figure 4: Kaplan-Meier survival function based on surgical procedure

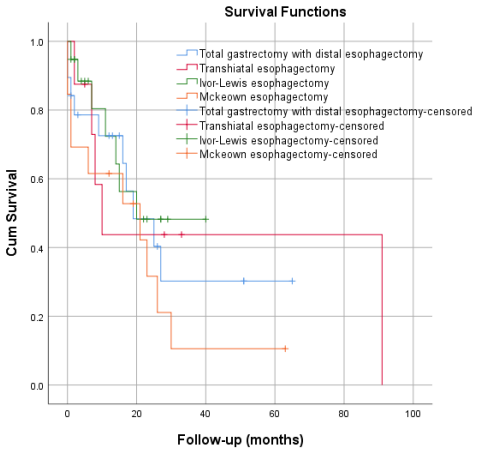
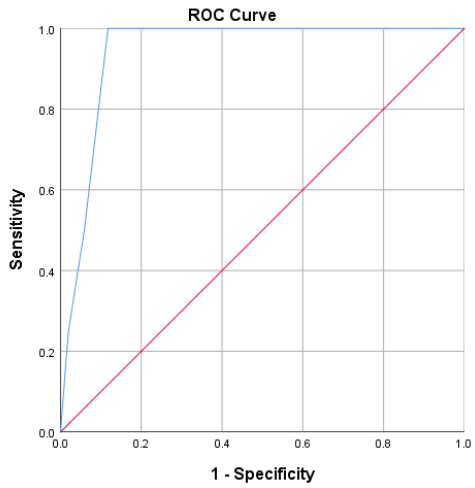


Figure 5: ROC curve for SAS against 30-day mortality



Discussion

This study provides a detailed analysis of survival outcomes following esophagectomy for esophageal and GEJ cancer at our institution. We evaluated multiple prognostic factors, including treatment strategies, tumor staging, surgical techniques, and perioperative risk assessments. Our findings reinforce the notion that survival outcomes are significantly influenced by the chosen treatment protocol, tumor pathology, and patient-specific factors such as age and comorbidities.

The overall 5-year survival rate of 32% that we observed is consistent with the previous literature, which has reported survival rates ranging between 15% and 50% depending on staging and treatment modalities [1,2]. Notably, patients in the perioperative chemotherapy (FLOT) group exhibited higher survival rates than patients in the primary surgery and neoadjuvant chemoradiotherapy (CROSS) groups. However, the differences among the groups were not statistically significant (P=0.121). The more positive outcomes observed in the FLOT cohort are consistent with recent trials that demonstrated the efficacy of perioperative chemotherapy at improving overall survival for gastroesophageal junction adenocarcinoma.6,14 However, additional longitudinal studies are necessary to ascertain the enduring nature of these findings and potential long-term complications associated with this approach.

One of the most influential prognostic factors identified in this study was postoperative pathological staging, which showed a clear inverse correlation with survival outcomes. Stage I patients exhibited a 52% 5-year survival rate; patients with stage III and IV diseases had significantly lower survival rates—no stage IV patients survived more than 2 months. These results corroborate previous findings that highlight early-stage disease as a key determinant of improved survival following esophagectomy [11]. Furthermore, the observation that patients achieving complete pathological response post-neoadjuvant therapy had a 75% survival rate suggests that tumor downstaging plays a critical role in improving survival rates [19,21].

Surgical technique also appeared to influence outcomes, with patients undergoing McKeown esophagectomy exhibiting the lowest 5-year survival rates (11%) compared with other procedures. However, this difference was not statistically significant (P=0.544). Complication rates, particularly anastomotic leaks, varied among the procedures; transhiatal esophagectomy exhibited the highest incidence of complications (i.e., 50%). Despite these complications, overall perioperative mortality was comparable across all of the surgical techniques. This finding highlights the importance of individual patient selection when determining the most appropriate surgical approach [7,13].

The implementation of the SAS in our cohort further validated its utility at predicting operative risk. The ROC curve analysis (AUC=0.94) suggests that SAS may serve as a robust tool for identifying high-risk patients who may benefit from intensified perioperative monitoring. This finding is consistent with previous studies demonstrating the predictive value of SAS in gastrointestinal surgeries [15,17].

While our study contributes to the growing debate regarding the necessity of immediate surgery following neoadjuvant therapy, it also has several limitations. First, its single-center, non-randomized design inherently introduces selection bias, particularly in the allocation of treatment strategies; treatment strategies were based on clinical judgment rather than standardized randomization. Second, the relatively small sample size of our cohort, especially when stratified across three distinct treatment arms and multiple surgical techniques, limits our statistical power to detect significant differences in survival outcomes. Additionally, heterogeneity in tumor histology and location, while reflective of real-world clinical practice, may have confounded direct comparisons among the groups. Lastly, although the SAS exhibited strong predictive value in our patient population its generalizability still remains uncertain. Multi-center prospective studies with larger cohorts and longer follow-up durations are necessary to validate these findings and explore the

integration of SAS into routine preoperative assessment algorithms to enhance surgical risk stratification.

Conclusions

This study underscores the complexity of managing esophageal and gastroesophageal junction cancers and reveals the significant impact of pathological staging on postoperative survival outcomes. Our findings show that postoperative pathological staging remains the strongest predictor of survival, confirming that earlier stages correlate with better prognoses. The use of perioperative chemotherapy, particularly the FLOT protocol, is correlated with improved survival outcomes, suggesting a potential shift in treatment paradigms for these malignancies. However, we did not measure statistically significant differences among the groups, which highlights the need for additional research.

Moreover, the SAS has shown to be a valuable predictor of perioperative risk; it offers a reliable way of anticipating patient outcomes post-surgery. The variation in survival rates among the various surgical techniques, although not statistically significant, suggests that individual surgical approaches should be tailored based on specific patient and disease characteristics.

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