Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Survival and Complication Patterns Following Transhiatal Esophagectomy in Patients with Locally Advanced Esophagogastric Junction Adenocarcinoma

Amirmasoud Karimi
Alborz University of Medical Sciences
Mojtaba Ahmadinezhad
Alborz University of Medical Sciences
Seyed Alireza Hosseini
Alborz University of Medical Sciences
Shima Ahmadikia
Alborz University of Medical Sciences
Amirhossein Hajialigol
ah.hajialigol@gmail.com

Alborz Office of Universal Scientific Education and Research Network (USERN), Alborz University of Medical Sciences
Sanaz Mohammadzadeh
Alborz University of Medical Sciences
Izadmehr Ahmadinejad
Tehran University of Medical Sciences

Research Article

Keywords: Esophagogastric junction adenocarcinoma, Transhiatal esophagectomy, Postoperative complications, Overall survival, Disease-free survival, Prognostic factors

Posted Date: June 28th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9960149/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Adenocarcinoma of the esophagogastric junction (EGJ) is frequently diagnosed at an advanced stage and remains associated with considerable postoperative morbidity and limited long-term survival. Transhiatal esophagectomy is an established curative-intent surgical approach, but patient selection, perioperative risk factors, and stage-specific outcomes require further evaluation in real-world clinical settings. This study aimed to assess postoperative complications, survival outcomes, and prognostic factors in patients with locally advanced EGJ adenocarcinoma undergoing transhiatal esophagectomy.

Methods

This retrospective cohort study included patients with locally advanced Siewert type I EGJ adenocarcinoma who underwent transhiatal esophagectomy at two tertiary referral hospitals between 2019 and 2022. Demographic, clinical, operative, pathological, and follow-up data were extracted from hospital records. Postoperative complications were classified using the Clavien–Dindo system, and esophagectomy-specific complications were recorded according to accepted definitions. Overall survival and disease-free survival were estimated using Kaplan–Meier analysis. Logistic regression was used to identify predictors of postoperative complications, and regression models were applied to evaluate factors associated with survival outcomes.

Results

A total of 101 patients were included: 65 men (64.4%) and 36 women (35.6%), with a mean age of 63.4 ± 8.9 years and mean BMI of 27.05 ± 4.12 kg/m². The 90-day morbidity rate was 47.5%, and the 90-day mortality rate was 7.9%. R0 resection was achieved in 95% of patients. Overall survival differed significantly by pathological stage, with 3-year survival rates of 68% for Stage 0, 60% for Stage I, 44% for Stage II, and 40% for Stage III disease ($p = 0.001$). Disease-free survival was also significantly better in earlier-stage disease compared with advanced-stage disease ($p < 0.001$). Significant predictors of early complications included hypoalbuminemia, comorbidities, smoking history, advanced clinical tumor stage, neoadjuvant chemoradiotherapy, and perioperative transfusion. Advanced TNM stage was the strongest predictor of poorer overall and disease-free survival.

Conclusion

Transhiatal esophagectomy provided acceptable oncologic outcomes in patients with locally advanced EGJ adenocarcinoma, although postoperative morbidity remained substantial. Nutritional status, smoking history, comorbidity burden, and pathological stage appear to be clinically important factors for

risk stratification. Careful preoperative optimization and multidisciplinary perioperative planning may improve surgical safety and long-term outcomes in this high-risk population.

1. Introduction

Esophagogastric junction (EGJ) adenocarcinoma represents a growing global health challenge, with its incidence steadily rising in both developed and developing countries. This malignancy emerges at the anatomical transition between the esophagus and stomach, an area highly susceptible to chronic acid reflux and obesity-related pathologies(1). Despite advances in diagnostic modalities, the majority of patients are still diagnosed at advanced stages, often limiting treatment options and leading to poor prognoses. The five-year survival rate, even with surgery, remains discouragingly low, underscoring the urgent need for optimized therapeutic strategies(2). Over the past decades, classification systems such as the Siewert classification have been introduced to better define tumors of the EGJ and guide surgical planning. According to this system, tumors are categorized into three types based on their epicenter in relation to the EGJ(3). However, in real-world clinical practice, determining the exact tumor location is not always straightforward, and biological similarities between the subtypes add to the complexity. These challenges complicate both treatment decision-making and research efforts, particularly when attempting to standardize surgical approaches and outcomes reporting(3).

Surgical resection continues to serve as the cornerstone of curative-intent treatment for localized EGJ adenocarcinoma. Historically, transhiatal esophagectomy (THE), popularized as an alternative to the Ivor Lewis approach, was introduced to reduce pulmonary complications associated with thoracotomy(3). By avoiding a chest incision and performing an anastomosis in the cervical region, THE was believed to reduce postoperative morbidity while maintaining oncologic efficacy. However, as with any complex surgical procedure, THE carries risks including anastomotic leak, pulmonary complications, and recurrent laryngeal nerve injury that remain significant concerns for surgeons and patients alike(4, 5). The evolution of multimodal strategies, including neoadjuvant chemotherapy and chemoradiotherapy, has further improved survival outcomes by targeting micrometastatic disease and enhancing resectability. Landmark trials, such as the CROSS study, have established combined-modality regimens as standard of care for many patients. Nevertheless, even in the era of multimodal therapy, surgery remains indispensable, and the choice of surgical technique (transhiatal versus transthoracic) continues to be debated. Both approaches have demonstrated comparable long-term survival in many analyses, but they differ in perioperative risk profiles, complication rates, and postoperative quality of life outcomes(6).

Given these considerations, evaluating the outcomes of transhiatal esophagectomy in real-world clinical practice remains crucial. Understanding the spectrum of postoperative complications, their predictors, and their impact on both survival and quality of life can help refine surgical strategies and optimize patient care. This study seeks to contribute to this ongoing discussion by analyzing the clinical, pathological, and surgical variables influencing postoperative results in patients with advanced, localized EGJ adenocarcinoma who underwent transhiatal esophagectomy in referral hospitals. By identifying key

prognostic factors, the findings may guide surgeons in tailoring operative techniques and perioperative management to achieve safer and more effective outcomes for this challenging disease.

2. Materials and methods

2.1. Study Design, Setting, and Participants

This retrospective cohort study was conducted to evaluate postoperative outcomes and prognostic factors in patients with locally advanced adenocarcinoma of the esophagogastric junction who underwent transhiatal esophagectomy. The study was designed and reported in accordance with the STROBE recommendations for observational cohort studies. The main outcomes of interest were postoperative complications, 90-day mortality, overall survival, and disease-free survival.

Patient data were obtained from the medical records of two tertiary referral hospitals in Karaj, Iran: Imam Ali Hospital and Shahid Madani Hospital. These centers provide surgical oncology care for patients with upper gastrointestinal malignancies. The study period covered patients treated between 2019 and 2022. Data collection included the preoperative, operative, postoperative, pathological, and follow-up phases of care. Eligible patients were adults aged 18 years or older with histologically confirmed, locally advanced adenocarcinoma of the esophagogastric junction who underwent transhiatal esophagectomy with curative intent. Patients were included if preoperative assessment classified the tumor as Siewert type I and showed no evidence of distant metastasis. Patients also needed to have sufficient clinical fitness to tolerate major surgery based on the multidisciplinary team assessment. Patients were excluded if they had Siewert type II or III tumors, distant metastatic disease, a history of previous esophageal or gastric surgery, incomplete medical records, or unavailable follow-up data. Because this was a retrospective study based on existing hospital records, the final study size was determined by the number of eligible patients treated during the study period rather than by prospective sample-size recruitment.

2.2. Preoperative Assessment, Variables, and Surgical Management

All patients underwent routine staging and preoperative evaluation before surgery. Diagnostic work-up included upper gastrointestinal endoscopy with biopsy, endoscopic ultrasonography when available, and thoracoabdominal computed tomography. Positron emission tomography/computed tomography was performed selectively when further staging clarification was needed. Tumor classification, treatment planning, and surgical eligibility were reviewed through multidisciplinary decision-making. The collected variables included demographic characteristics, baseline clinical status, comorbidities, nutritional status, tumor-related variables, treatment details, operative findings, pathological results, and postoperative outcomes. Age, sex, body mass index, serum albumin level, American Society of Anesthesiologists score, smoking history, reflux history, diabetes, cardiovascular disease, and pulmonary disease were recorded as baseline clinical variables. Treatment-related variables included receipt of neoadjuvant

chemotherapy or chemoradiotherapy, interval reassessment before surgery, operative time, estimated blood loss, and need for perioperative blood transfusion.

Neoadjuvant therapy was administered according to multidisciplinary tumor board recommendations. Treatment generally included platinum- and fluorouracil-based chemotherapy, either alone or combined with concurrent radiotherapy when clinically indicated. After completion of neoadjuvant treatment, patients were restaged to confirm the absence of disease progression and to determine final eligibility for surgical resection. Transhiatal esophagectomy was performed by experienced gastrointestinal surgeons using abdominal and cervical incisions without thoracotomy. The stomach was mobilized and fashioned as a conduit, then brought up for cervical esophagogastric anastomosis. Anastomotic reinforcement was performed when judged appropriate by the operating surgeon. Intraoperative variables, including operative duration, blood loss, and transfusion requirement, were documented from operative and anesthesia records.

2.3.Outcomes, Follow-up, and Statistical Analysis

Postoperative care followed institutional protocols. Patients were routinely admitted to the intensive care unit after surgery for hemodynamic and respiratory monitoring. Early mobilization, respiratory physiotherapy, pain control, and nutritional support were initiated as soon as clinically feasible. Postoperative complications were identified from inpatient records, operative notes, imaging reports, outpatient visits, and follow-up documentation. Complications were grouped as early or late postoperative events. Early complications included anastomotic leak, atrial arrhythmia, pneumonia or aspiration, chylothorax, and recurrent laryngeal nerve palsy. Late complications included dysphagia, anastomotic stricture, delayed gastric emptying, bile reflux, dumping syndrome, and malabsorption. Complication severity was graded using the Clavien–Dindo classification, and esophagectomy-specific complications were defined according to internationally accepted criteria, including the Esophagectomy Complications Consensus Group definitions where applicable.

Pathological variables were extracted from final surgical pathology reports. These included tumor depth, nodal status, pathological stage, tumor differentiation, resection margin status, total number of retrieved lymph nodes, and number of positive lymph nodes. Resection margins were classified as R0 when no microscopic residual tumor was present and R1 when microscopic residual disease was identified. Survival outcomes were defined as overall survival and disease-free survival. Overall survival was calculated from the date of surgery to death from any cause or last follow-up. Disease-free survival was calculated from the date of surgery to documented recurrence, death, or last disease-free follow-up. Descriptive statistics were used to summarize baseline, clinical, operative, and pathological variables. Continuous variables were reported as mean with standard deviation or median with range, depending on distribution. Categorical variables were reported as frequencies and percentages. Kaplan–Meier analysis was used to estimate overall and disease-free survival, and survival differences between pathological stage groups were assessed using the log-rank test.

Logistic regression models were used to evaluate predictors of early and late postoperative complications. Cox proportional hazards regression was used to assess factors associated with overall survival and disease-free survival. Variables of clinical relevance, including nutritional status, comorbidities, smoking history, tumor stage, neoadjuvant treatment, transfusion requirement, ASA score, and lymph node yield, were considered in the regression analyses. Results were reported using odds ratios or hazard ratios with 95% confidence intervals where appropriate. A two-sided p value below 0.05 was considered statistically significant. To reduce information bias, data were extracted from standardized hospital records and cross-checked against operative, pathology, and follow-up documentation when available. Patients with incomplete core data or unavailable follow-up were excluded from the final analysis. Statistical analyses were performed using SPSS version 26. The study protocol was approved by the ethics committee of Alborz University of Medical Sciences. Patient confidentiality was preserved throughout data extraction and analysis, and all data were anonymized before statistical evaluation.

3. Results

3.1.Patient Characteristics and Perioperative Profile

A total of 101 patients with locally advanced adenocarcinoma of the esophagogastric junction underwent transhiatal esophagectomy during the study period and were included in the final analysis. The cohort consisted of 65 men (64.4%) and 36 women (35.6%). The mean age was 63.4 ± 8.9 years, with an age range of 26 to 81 years. The mean body mass index was 27.05 ± 4.12 kg/m², ranging from 15.6 to 37 kg/m². Baseline demographic and clinical characteristics are summarized in Table 1.

Table 1
Demographic and Clinical Characteristics of Patients (n = 101)

Variable	N (%) / Mean ± SD (Range)
Male	65 (64.4%)
Female	36 (35.6%)
Age (years)	63.4 ± 8.9 (26–81)
BMI (kg/m²)	27.05 ± 4.12 (15.6–37)
Albumin < 3.5 g/dL	45 (44.6%)
Albumin ≥ 3.5 g/dL	56 (55.4%)
ASA I	10 (9.9%)
ASA II	76 (75.2%)
ASA III	15 (14.9%)
Cardiac comorbidity	45 (44.6%)
Vascular comorbidity	21 (20.8%)
Pulmonary comorbidity	15 (14.9%)
Diabetes	15 (14.9%)
Smoking history	70 (69.3%)
Reflux history	25 (24.8%)
Neoadjuvant chemotherapy	56 (55.4%)
Neoadjuvant chemoradiotherapy	25 (24.8%)
No neoadjuvant therapy	20 (19.8%)

Nutritional impairment was common in this cohort. Hypoalbuminemia, defined as serum albumin below 3.5 g/dL, was present in 45 patients (44.6%), while 56 patients (55.4%) had normal albumin levels. Most patients were classified as ASA II (75.2%), while 9.9% were ASA I and 14.9% were ASA III. The most frequent comorbid condition was cardiovascular disease, observed in 44.6% of patients. Diabetes and pulmonary disease were each reported in 14.9% of patients. A history of smoking was documented in 69.3%, and reflux disease was reported in 24.8% of patients. Preoperative treatment was administered according to multidisciplinary decision-making. Neoadjuvant chemotherapy was given to 55.4% of patients, while 24.8% received neoadjuvant chemoradiotherapy. The remaining 19.8% underwent surgery without preoperative oncologic treatment. Operatively, the mean duration of surgery was 200 minutes, with a range of 180 to 400 minutes. Mean estimated blood loss was 250 mL, ranging from 0 to 3000 mL, and 14 patients (13.9%) required intraoperative blood transfusion (Table 1).

3.2.Postoperative Complications and Pathological Outcomes

Early postoperative complications were recorded within the perioperative period and are shown in Table 2. The most frequent early complication was pneumonia or aspiration, which occurred in 14.85% of patients. Atrial arrhythmia was observed in 7.92%, while anastomotic leak and recurrent laryngeal nerve palsy each occurred in 3.96% of patients. Chylothorax was less common and was reported in 1.98% of cases. Overall, 47.5% of patients developed morbidity within 90 days after surgery. Late postoperative complications were also frequent and are detailed in Table 2. Malabsorption was the most common late event, affecting 35.64% of patients, followed by delayed gastric emptying in 23.76% and dysphagia in 18.81%. Dumping syndrome occurred in 13.86%, bile reflux in 10.89%, and anastomotic stricture in 7.92% of patients. According to the Clavien–Dindo classification, 29.7% of patients had grade I/II complications, 13.86% had grade IIIa/IIIb complications, and 4.95% had grade IV complications. The 90-day mortality rate was 7.9% (Table 2).

Table 2
Postoperative Complications and Outcomes

Complication / Outcome	N (%)
Early complications	
Anastomotic leak	4 (3.96%)
Atrial arrhythmia	8 (7.92%)
Pneumonia / Aspiration	15 (14.85%)
Chylothorax	2 (1.98%)
Recurrent nerve palsy	4 (3.96%)
Late complications	
Dysphagia	19 (18.81%)
Anastomotic stricture	8 (7.92%)
Delayed gastric emptying	24 (23.76%)
Bile reflux	11 (10.89%)
Dumping syndrome	14 (13.86%)
Malabsorption	36 (35.64%)
Other outcomes	
Reoperation	11 (10.89%)
Readmission	15 (14.85%)
Clavien–Dindo Grade I/II	30 (29.7%)
Clavien–Dindo Grade IIIa/IIIb	14 (13.86%)
Clavien–Dindo Grade IV	5 (4.95%)
90-day mortality	8 (7.92%)

Final pathological assessment showed that R0 resection was achieved in 95% of patients, while 5% had microscopic residual disease classified as R1. The mean number of retrieved lymph nodes was 11, with a range of 6 to 26, and the mean number of positive lymph nodes was 3, ranging from 1 to 15. Pathological tumor staging showed pT0–Tis in 15.8%, pT1 in 22.8%, pT2 in 52.5%, pT3 in 6.9%, and pT4 in 2.0% of patients. Nodal staging was pN0 in 66.3%, pN1 in 24.7%, and pN2 in 8.9%. Overall pathological stage was Stage 0 in 21.7%, Stage I in 12.8%, Stage II in 33.7%, and Stage III in 31.7%. Tumor differentiation was well differentiated in 43.6%, moderately differentiated in 36.6%, poorly differentiated in 17.8%, and mucinous in 2.0% of cases (Table 3).

Table 3
Pathological Findings

Pathological Feature	N (%) / Mean (Range)
Tumor depth (pT)	
pT0–Tis	16 (15.8%)
pT1	23 (22.8%)
pT2	53 (52.5%)
pT3	7 (6.9%)
pT4	2 (2.0%)
Nodal status (pN)	
pN0	67 (66.3%)
pN1	25 (24.7%)
pN2	9 (8.9%)
Stage	
Stage 0	22 (21.7%)
Stage I	13 (12.8%)
Stage II	34 (33.7%)
Stage III	32 (31.7%)
Differentiation	
Well differentiated	44 (43.6%)
Moderately differentiated	37 (36.6%)
Poorly differentiated	18 (17.8%)
Mucinous	2 (2.0%)
Margins	
R0	96 (95%)
R1	5 (5%)
Lymph nodes	
Mean retrieved	11 (6–26)
Mean positive	3 (1–15)

3.3.Survival Outcomes and Predictors of Complications

Survival outcomes differed significantly according to pathological stage. At 1-year, overall survival was 90% for Stage 0, 85% for Stage I, 68% for Stage II, and 40% for Stage III disease. At 3 years, overall survival decreased to 68% for Stage 0, 60% for Stage I, 44% for Stage II, and 40% for Stage III. The Kaplan–Meier analysis demonstrated a statistically significant difference in overall survival across pathological stages, with a log-rank p value of 0.001 (Fig. 1; Table 4).

Table 4
Multivariate Cox Regression for Overall Survival (OS)

Variable	Hazard Ratio (HR) (95% CI)	p-value
ASA (3–4 vs. 1–2)	0.89 (0.34–2.34)	0.81
TNM stage (III–IV vs. 0–II)	3.39 (1.88–6.12)	< 0.001*
Lymph nodes retrieved ≥ 10 vs < 10	0.72 (0.39–1.31)	0.28
*Significant at p < 0.001		

Disease-free survival also showed a clear stage-related pattern. Patients with Stage 0–I disease had better disease-free survival than those with Stage II–III disease. Disease-free survival was 90% at 6 months and 70% at 18 months among patients with Stage 0–I disease, compared with 60% and 54%, respectively, among those with Stage II–III disease. This difference was statistically significant, with p < 0.001, confirming the strong association between disease stage and recurrence-free outcome (Fig. 2; Table 5).

Table 5
Multivariate Cox Regression for Disease-Free Survival (DFS)

Variable	Hazard Ratio (HR) (95% CI)	p-value
ASA (3–4 vs. 1–2)	0.87 (0.25–3.02)	0.82
TNM stage (III–IV vs. 0–II)	3.94 (1.92–8.09)	< 0.001*
Lymph nodes retrieved ≥ 10 vs < 10	0.60 (0.30–1.20)	0.15
*Significant at p < 0.001		

Regression analyses identified several predictors of postoperative complications and survival. Early complications were significantly associated with hypoalbuminemia (OR = 1.5, p = 0.04), comorbidities (OR = 1.5, p = 0.03), smoking history (OR = 1.7, p = 0.03), clinical tumor stage ≥ cT2 (OR = 1.6, p = 0.02), neoadjuvant chemoradiotherapy (OR = 2.0, p = 0.01), and perioperative transfusion (OR = 1.0, p = 0.02) (Table 6). Predictors of late complications included comorbidities (OR = 1.4, p = 0.02), advanced T stage (OR = 1.8, p = 0.01), and higher Clavien–Dindo grade morbidity (OR = 2.3, p = 0.01) (Table 7). In survival analysis, advanced TNM stage was the strongest independent predictor of worse outcome. Patients with

Stage III–IV disease had significantly poorer overall survival (HR = 3.39, 95% CI: 1.88–6.12, p < 0.001) and disease-free survival (HR = 3.94, 95% CI: 1.92–8.09, p < 0.001) compared with patients with Stage 0–II disease. ASA score and lymph node yield, categorized as ≥ 10 versus < 10 retrieved nodes, were not significantly associated with survival outcomes .

Table 6
Logistic Regression Analysis of Demographic and Clinical Variables for Early Postoperative Complications

Variable	**Odds Ratio (95% CI)**	**p-value**
Sex (Male vs. Female)	1.1	0.62
Age	0.99	0.76
BMI	1.02	0.88
Albumin (< 3.5 g/dL)	1.5	0.04*
ASA score	0.95	0.84
Comorbidities (any)	1.5	0.03*
Smoking history	1.7	0.03*
Tumor stage ≥cT2	1.6	0.02*
Neoadjuvant chemoradiotherapy	2.0	0.01*
90-day morbidity (Grade III/IV)	2.1	0.01*
Blood transfusion (yes)	1.0	0.02*
Operative time	1.00	0.97
90-day mortality	0.8	0.77
*Significant at p < 0.05		

Table 7
Logistic Regression Analysis of Demographic and Clinical Variables for Late Postoperative Complications

Variable	Odds Ratio (95% CI)	p-value
Sex (Male vs. Female)	1.0	0.95
Age	1.01	0.93
BMI	0.99	0.82
Albumin (< 3.5 g/dL)	1.2	0.31
ASA score	0.97	0.76
Comorbidities (any)	1.4	0.02*
Smoking history	1.1	0.56
Tumor stage ≥cT2	1.8	0.01*
Neoadjuvant chemoradiotherapy	1.1	0.62
90-day morbidity (Grade III/IV)	2.3	0.01*
Blood transfusion (yes)	1.0	0.99
Operative time	1.00	0.99
90-day mortality	0.9	0.82
*Significant at p < 0.05		

4. Discussion

This retrospective cohort study evaluated postoperative complications, pathological outcomes, and survival patterns after transhiatal esophagectomy in patients with locally advanced esophagogastric junction adenocarcinoma. The main findings were that postoperative morbidity remained substantial, while oncologic outcomes were acceptable in the context of a high-risk surgical population. The 90-day morbidity rate was 47.5%, and the 90-day mortality rate was 7.9%. R0 resection was achieved in 95% of patients, suggesting that transhiatal esophagectomy can provide adequate margin clearance in selected patients. Survival was strongly stage-dependent: 3-year overall survival was 68% for Stage 0, 60% for Stage I, 44% for Stage II, and 40% for Stage III disease, with a significant difference across pathological stages ($p = 0.001$). Disease-free survival was also significantly better in early-stage disease than in advanced-stage disease ($p < 0.001$).

Postoperative morbidity remains one of the most important challenges after esophagectomy. Reported complication rates vary widely across studies, partly because of differences in patient selection, surgical approach, definitions of complications, and reporting systems (7, 8). In the present study, complications were classified using the Clavien–Dindo system, with esophagectomy-specific events defined according

to accepted criteria, including the Esophagectomy Complications Consensus Group framework where applicable (9).This approach improves comparability and reduces ambiguity in outcome reporting. The observed 90-day morbidity rate of 47.5% is consistent with previous reports of substantial postoperative morbidity after esophagectomy, including studies of transhiatal and transthoracic resections (10, 11). The 90-day mortality rate of 7.9% is also within the range reported in high-risk esophagectomy cohorts, although it remains clinically meaningful and underscores the need for careful perioperative risk management (12, 13).

The pattern of complications in this cohort reflects the known morbidity profile of esophagectomy. Pneumonia or aspiration was the most common early complication, affecting 14.85% of patients, followed by atrial arrhythmia, anastomotic leak, recurrent laryngeal nerve palsy, and chylothorax. Late complications were also frequent, particularly malabsorption, delayed gastric emptying, and dysphagia. These findings are clinically important because both early and late complications can delay recovery, prolong hospitalization, impair nutritional rehabilitation, and reduce quality of life. Although cervical anastomosis may reduce the severity of intrathoracic septic complications, it does not eliminate the risk of anastomotic leak or functional sequelae. Therefore, systematic postoperative surveillance, early respiratory physiotherapy, nutritional support, and structured follow-up should be considered essential components of care after transhiatal esophagectomy.

Survival outcomes were closely related to pathological stage, which remained the dominant prognostic factor in this cohort. Patients with earlier-stage disease had clearly better overall and disease-free survival than those with more advanced disease. This finding is consistent with previous evidence showing that pathological stage is among the strongest determinants of long-term outcomes after resection for esophageal and esophagogastric junction cancer (14, 15). In the present study, advanced TNM stage was associated with significantly worse overall survival and disease-free survival. Patients with Stage III–IV disease had poorer overall survival compared with those with Stage 0–II disease, and a similar pattern was observed for disease-free survival. These findings reinforce the importance of accurate staging before treatment, appropriate use of neoadjuvant therapy, and close postoperative surveillance in patients with advanced tumors. Disease-free survival also showed a clear stage-related gradient. Patients with Stage 0–I disease had higher disease-free survival than those with Stage II–III disease, with statistically significant separation between the groups ($p < 0.001$). This observation is consistent with prior reports showing that recurrence risk increases with more advanced pathological stage, nodal involvement, and adverse tumor biology (16, 17). In clinical practice, this supports tailoring follow-up intensity according to pathological risk. Patients with advanced-stage disease may benefit from closer surveillance, early imaging when clinically indicated, and consideration of additional systemic treatment strategies based on multidisciplinary review.

Pathological outcomes in this cohort were encouraging. R0 resection was achieved in 95% of patients, while R1 resection was observed in only 5%. Critics of transhiatal esophagectomy have argued that this approach may provide less extensive mediastinal exposure than transthoracic esophagectomy, particularly in more advanced tumors or tumors with mediastinal extension (18, 19). However, the low

rate of positive margins in this study suggests that, in carefully selected patients with Siewert type I tumors, transhiatal esophagectomy can achieve acceptable oncologic clearance. The mean number of retrieved lymph nodes was 11, which provides useful staging information, although the adequacy of lymphadenectomy should still be interpreted in light of institutional technique, tumor location, neoadjuvant therapy, and pathological processing (20, 21).

Nutritional status emerged as an important and modifiable factor associated with postoperative risk. Hypoalbuminemia was significantly associated with early postoperative complications (OR = 1.5, p = 0.04). This finding is biologically plausible, as low serum albumin may reflect malnutrition, systemic inflammation, impaired healing capacity, and reduced physiological reserve. Previous studies have similarly reported that poor nutritional status is associated with higher postoperative morbidity, prolonged hospitalization, and worse recovery after foregut cancer surgery (22, 23). These findings support routine preoperative nutritional assessment and optimization before esophagectomy. When feasible, patients with malnutrition or hypoalbuminemia should receive structured nutritional support before surgery as part of a multidisciplinary prehabilitation pathway.

Comorbidity burden and smoking history were also associated with early postoperative complications. Patients with comorbidities had a higher risk of early complications (OR = 1.5, p = 0.03), and smoking history was likewise significant (OR = 1.7, p = 0.03). These findings are consistent with the clinical expectation that cardiovascular, pulmonary, and metabolic disease reduce physiological reserve after major surgery. Smoking may further increase risk through impaired mucociliary clearance, reduced pulmonary function, impaired tissue oxygenation, and delayed wound healing. These results support active preoperative optimization, including smoking cessation, cardiopulmonary assessment, respiratory training, glycemic control, and individualized anesthetic planning.

Treatment- and procedure-related factors also influenced postoperative outcomes. Neoadjuvant chemoradiotherapy was associated with early complications (OR = 2.0, p = 0.01), and perioperative transfusion was also significantly associated with early morbidity (OR = 1.0, p = 0.02). The association between neoadjuvant chemoradiotherapy and complications may reflect treatment-related tissue effects, baseline disease severity, or selection of patients with more advanced tumors. Similarly, blood transfusion may act as a marker of operative complexity, blood loss, frailty, or perioperative instability rather than a purely causal factor. Nevertheless, these findings support meticulous operative technique, careful blood conservation strategies, and judicious transfusion practice within enhanced recovery pathways.

Late complications were associated with comorbidities, advanced T stage, and higher-grade early morbidity. Comorbidities increased the risk of late complications (OR = 1.4, p = 0.02), while tumor stage ≥ cT2 was also significant (OR = 1.8, p = 0.01). Higher Clavien–Dindo grade morbidity was associated with later complications as well (OR = 2.3, p = 0.01). These findings suggest that the consequences of esophagectomy extend beyond the immediate postoperative period. Patients who experience severe early complications may require longer follow-up, nutritional monitoring, swallowing assessment, and

early management of functional sequelae such as dysphagia, reflux, delayed gastric emptying, and malabsorption.

This study has several limitations that should be considered when interpreting the findings. First, its retrospective design introduces a risk of information bias, particularly for variables dependent on the completeness and accuracy of hospital records. Although data were extracted from standardized medical, operative, pathology, and follow-up documents, residual misclassification remains possible. Second, the study was conducted in two referral centers within a single geographic region, which may limit external validity. Third, the sample size was modest, and this may have limited the statistical power to detect weaker associations or to perform detailed subgroup analyses. Fourth, patients with incomplete records or unavailable follow-up were excluded, which could introduce selection bias if excluded patients differed systematically from those included in the analysis. Additional limitations relate to treatment heterogeneity and follow-up. Some patients received neoadjuvant chemotherapy, some received chemoradiotherapy, and others proceeded directly to surgery. Although this reflects real-world multidisciplinary practice, it may complicate interpretation of survival and complication patterns. Follow-up duration and surveillance intensity may also have varied between patients. Moreover, quality-of-life outcomes, nutritional recovery, functional swallowing status, and patient-reported outcomes were not comprehensively analyzed. These endpoints are particularly relevant after esophagectomy and should be incorporated into future prospective studies.

Despite these limitations, the study provides useful real-world evidence on transhiatal esophagectomy for locally advanced esophagogastric junction adenocarcinoma. The findings are most generalizable to patients with Siewert type I EGJ adenocarcinoma treated in tertiary referral centers with access to multidisciplinary evaluation, experienced gastrointestinal surgeons, intensive postoperative care, and structured pathology reporting. Caution is needed when extrapolating these results to lower-volume centers, patients with Siewert type II or III tumors, patients with metastatic disease, or those undergoing different surgical approaches such as transthoracic or minimally invasive esophagectomy.

Overall, this study shows that transhiatal esophagectomy can achieve acceptable oncologic outcomes in selected patients with locally advanced EGJ adenocarcinoma, particularly when R0 resection is feasible. However, postoperative morbidity remains substantial and is influenced by nutritional status, comorbidities, smoking history, tumor stage, neoadjuvant treatment, and perioperative transfusion. These findings support careful preoperative risk stratification, nutritional optimization, smoking cessation, multidisciplinary treatment planning, and structured postoperative follow-up. Future multicenter prospective studies are needed to validate these findings, compare transhiatal and transthoracic approaches using standardized definitions, and evaluate long-term quality of life alongside survival outcomes.

Abbreviations

ASA: American Society of Anesthesiologists

BMI: Body Mass Index

CI: Confidence Interval

CGEJ: Carcinoma of the Gastroesophageal Junction

CT: Computed Tomography

DFS: Disease-Free Survival

ECCG: Esophagectomy Complications Consensus Group

EGJ: Esophagogastric Junction

LN: Lymph Node

MRI: Magnetic Resonance Imaging

OR: Odds Ratio

OS: Overall Survival

PET/CT: Positron Emission Tomography/Computed Tomography

R0/R1: Resection Margin Status (R0: negative; R1: microscopically positive)

SD: Standard Deviation

THE: Transhiatal Esophagectomy

TTE: Transthoracic Esophagectomy

TNM: Tumor–Node–Metastasis (staging system)

Declarations

Consent for publication: Not applicable

Ethics: Informed consent was obtained from all subjects and/or their legal guardian(s). All patients were briefed about the study aims and written consent was also obtained from all participants.

This study was approved in the ethical committee of Alborz University of medical sciences with code of IR.ABZUMS.REC.1402.300

https://ethics.research.ac.ir/EthicsProposalView.php?&code=IR.ABZUMS.REC.1402.300

Availability of data and material: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests

Funding: No funding was utilized for this manuscript.

Conflicts of interest: The authors have no conflicts of interest to disclose.

Authors' contributions: AK, SHA, IA, SM, and AH contributed to the data gathering, conceptualization, supervision, and writing the original draft; SAH, MA and AH reviewed and edited the final manuscript. All authors read and approved the final manuscript.

References

1. Nakagawa M, Nakajima M, Yoshimatsu M, Ueta Y, Inoue N, Ochiai T, Takise S, Fujita J, Morita S, Kojima K. An Overview of the Treatment Strategy of Esophagogastric Junction Cancer. Cancers. 2025;17(12):1961.
2. Schlottmann F, Casas MA, Molena D. Evidence-based approach to the treatment of esophagogastric junction tumors. World J Clin Oncol. 2022;13(3):159–67.
3. Zhang S, Orita H, Fukunaga T. Current surgical treatment of esophagogastric junction adenocarcinoma. World J Gastrointest Oncol. 2019;11(8):567–78.
4. Scheese D, Alwatari Y, Rustom S, He G, Puig CA, Julliard WA, Shah RD. Chest vs. neck anastomotic leak post esophagectomy for malignancy: rate, predictors, and outcomes. J Thorac Dis. 2023;15(7):3593–604.
5. Jiang M, Liang W, Chen X, Ge Y, Fang Y, Zhang H, Jiang R, Luo B. Effective management of cervical anastomotic leakage post-esophageal cancer surgery using negative pressure wound therapy with saline instillation: A case report. Asia Pac J Oncol Nurs. 2025;12:100623.
6. Barreto JC, Posner MC. Transhiatal versus transthoracic esophagectomy for esophageal cancer. World J Gastroenterol. 2010;16(30):3804–10.
7. Gritsiuta AI, Esper CJ, Parikh K, Parupudi S, Petrov RV.)Anastomotic Leak After Esophagectomy: Modern Approaches to Prevention and Diagnosis. Cureus. 2025;17(3):e80091.
8. Bona D, Manara M, Bonitta G, Guerrazzi G, Guraj J, Lombardo F, Biondi A, Cavalli M, Bruni PG, Campanelli G, Bonavina L, Aiolfi A. (2024)Long-Term Impact of Severe Postoperative Complications after Esophagectomy for Cancer: Individual Patient Data Meta-Analysis. Cancers (Basel) 16(8).
9. Bundred JR, Hollis AC, Evans R, Hodson J, Whiting JL, Griffiths EA. Impact of postoperative complications on survival after oesophagectomy for oesophageal cancer. BJS Open. 2020;4(3):405–15.
10. Rentz J, Bull D, Harpole D, Bailey S, Neumayer L, Pappas T, Krasnicka B, Henderson W, Daley J, Khuri S. (2003)Transthoracic versus transhiatal esophagectomy: a prospective study of 945 patients. J

Thorac Cardiovasc Surg 125(5):1114–20.

11. Yang Y, Han C, Xing X, Qin Z, Wang Q, Lan L, Zhu H. Effects of Postoperative Complications on Overall Survival Following Esophagectomy: A Meta-Analysis Using the Restricted Mean Survival Time Analysis. Thorac Cancer. 2025;16(3):e70011.
12. Weller J, Gutton J, Hocquet G, Pellet L, Aroulanda MJ, Bruandet A, Theis D, Boudis F, Cador R, Zweigenbaum P, Buronfosse A, de Groote P, Komajda M. Prediction of 90 day mortality in elderly patients with acute HF from e-health records using artificial intelligence. ESC Heart Fail. 2025;12(3):2200–9.
13. Goense L, Ruurda JP, van Hillergersberg R. Recent advances in defining and benchmarking complications after esophagectomy. J Thorac Dis. 2019;11(11):E243–6.
14. de Jesus VHF, da Costa WL Jr., Felismino TC, Calsavara VF, Diniz AL, de Castro Ribeiro HS, de Godoy AL, de Farias IC, Coimbra FJF. Survival outcomes of patients with pathological stage I gastric cancer using the competing risks survival method. J Gastrointest Oncol. 2019;10(6):1110–9.
15. Rodriguez-Quintero JH, Kamel MK, Jindani R, Elbahrawy M, Vimolratana M, Chudgar NP, Stiles BM. The Effect of Neoadjuvant Therapy on Esophagectomy for cT2N0M0 Esophageal Adenocarcinoma. Ann Surg Oncol. 2024;31(1):228–38.
16. Sargent DJ, Wieand HS, Haller DG, Gray R, Benedetti JK, Buyse M, Labianca R, Seitz JF, O'Callaghan CJ, Francini G, Grothey A, O'Connell M, Catalano PJ, Blanke CD, Kerr D, Green E, Wolmark N, Andre T, Goldberg RM, De Gramont A. Disease-free survival versus overall survival as a primary end point for adjuvant colon cancer studies: individual patient data from 20,898 patients on 18 randomized trials. J Clin Oncol. 2005;23(34):8664–70.
17. Koterazawa Y, Oshikiri T, Goto H, Kato T, Sawada R, Harada H, Urakawa N, Hasegawa H, Kanaji S, Yamashita K, Matsuda T, Kakeji Y. (2024)Impact of Tumor Size on Survival Outcome in Esophageal Squamous Cell Carcinoma After Esophagectomy Following Neoadjuvant Chemotherapy. Ann Surg Oncol 31(4):2482–9.
18. Mülküt F, Ofluoğlu CB, Başdoğan MK, Aydın İC, Doğan A, Subaşı İE. (2025)Prognostic and Inflammatory Differences Between Upper and Mid-Lower Rectal Cancers in Non-Metastatic Stage II-III Disease. Curr Oncol 32(4).
19. Soltani E, Mahmoodzadeh H, Jabbari Nooghabi A, Jabbari Nooghabi M, Ravankhah Moghaddam K, Hassanzadeh Haddad E. Transhiatal versus transthoracic esophagectomy for esophageal SCC: outcomes and complications. J Cardiothorac Surg. 2022;17(1):150.
20. Pang T, Nie M, Yin K. The correlation between the margin of resection and prognosis in esophagogastric junction adenocarcinoma. World J Surg Oncol. 2023;21(1):316.
21. Boerner T, Carr R, Hsu M, Tan KS, Sigel C, Tang L, Harrington C, Ku GY, Ilson DH, Janjigian YY, Wu AJ, Sihag S, Bains MS, Bott MJ, Isbell JM, Park BJ, Jones DR, Molena D. Prognostic value of circumferential radial margin involvement in esophagectomy for esophageal cancer: a case series. Int J Surg. 2023;109(11):3251–61.

22. Poziomyck AK, Weston AC, Lameu EB, Cassol OS, Coelho LJ, Moreira LF. Preoperative nutritional assessment and prognosis in patients with foregut tumors. Nutr Cancer. 2012;64(8):1174–81.
23. Marin FA, Lamônica-Garcia VC, Henry MA, Burini RC. Grade of esophageal cancer and nutritional status impact on postsurgery outcomes. Arq Gastroenterol. 2010;47(4):348–53.

Figures

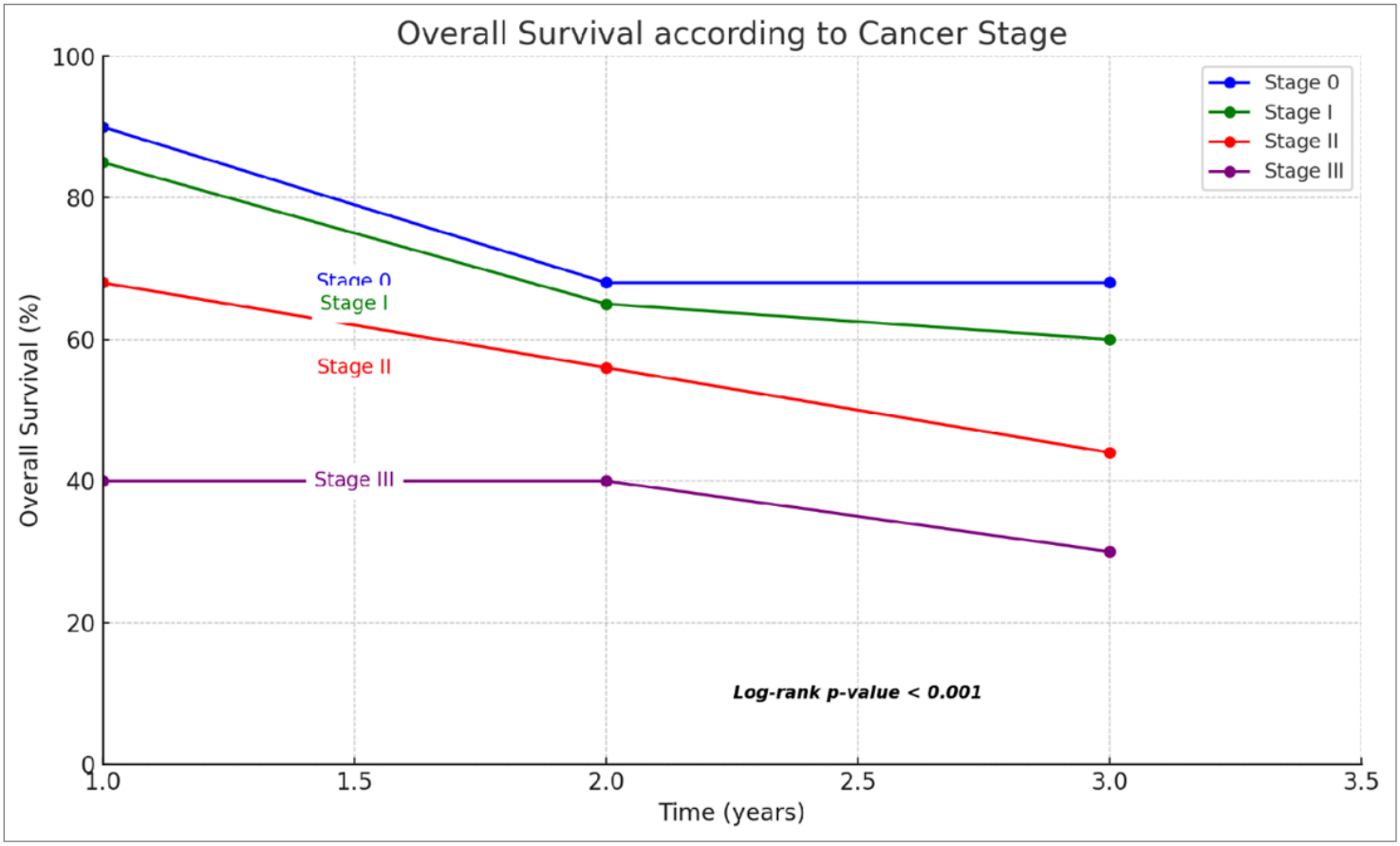


Figure 1

Kaplan-Meier curve for overall survival after transhiatal esophagectomy according to pathological stages of the disease.

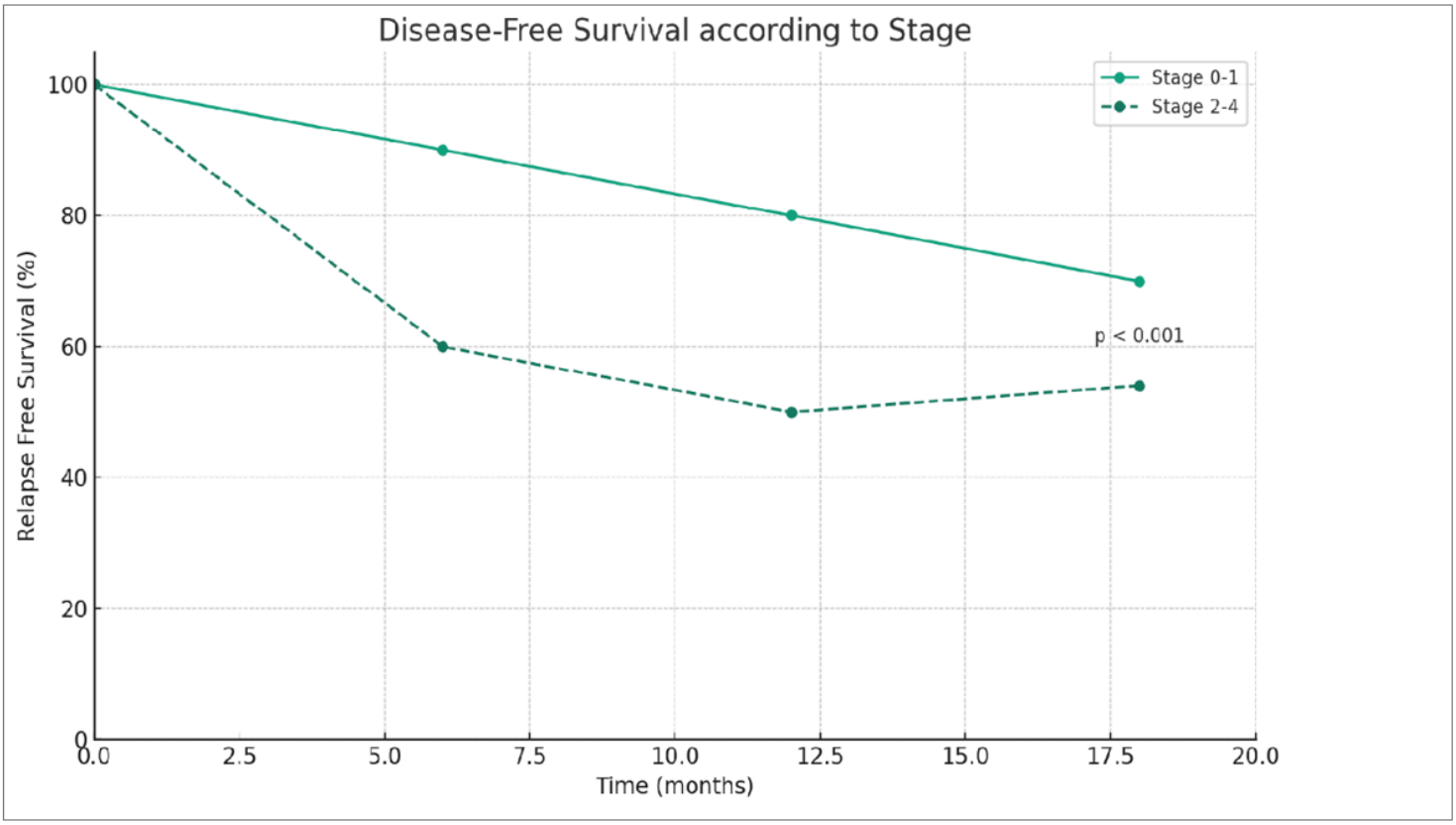


Figure 2

Kaplan-Meier curve for disease-free survival after transhiatal esophagectomy based on pathological stage