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Original Article

TPF regimen improves conversion surgery and short-term survival in patients with locally unresectable advanced gastric cancer

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Abstract: Objective: To compare the efficacy and safety of TPF versus FOLFOX regimens in conversion therapy for locally unresectable advanced gastric cancer (LAUGC) and to identify prognostic factors influencing clinical outcomes. Methods: This retrospective study analyzed 264 LAUGC patients treated with either TPF (n=140) or FOLFOX (n=124) between 2019 and 2021. Primary endpoints were objective response rate (ORR) and 1-year survival; secondary endpoints included conversion surgery rate, toxicity, and 3-year survival. Prognostic factors were evaluated using multivariate Cox regression and time-dependent ROC analyses. Results: The TPF group demonstrated significantly higher ORR (P=0.01) and disease control rate (DCR; P<0.001) compared to the FOLFOX group. Rates of conversion surgery (P=0.011) and R0 resection (P=0.003) were also improved. One-year survival was superior in the TPF cohort (P<0.05), whereas 3-year survival rates showed no significant difference (P>0.05). Although myelosuppression was more frequent with TPF (P=0.002), the incidence of severe adverse events was comparable between groups. Multivariate analysis identified FOLFOX regimen, elevated carcinoembryonic antigen (CEA), and N3 stage as risk factors for 1-year mortality, while higher albumin levels and lymphocyte counts were protective. Tumor size ≥5 cm and poor differentiation were associated with increased 3-year mortality risk. Albumin demonstrated strong predictive value for 1-year survival. Conclusion: The TPF regimen can effectively improve the objective response rate and short-term survival in LAUGC patients undergoing conversion therapy, with manageable myelosuppression. The analysis of prognostic risk factors facilitates individualized treatment strategies.

Keywords: Advanced gastric cancer, conversion therapy, paclitaxel, oxaliplatin, fluorouracil

Introduction

Gastric cancer remains one of the most prevalent and lethal malignancies worldwide. In 2020, an estimated 1.089 million new cases and 769,000 gastric cancer-related deaths were reported globally [1]. According to global cancer statistics, gastric cancer ranks as the fifth most common cancer and the fourth leading cause of cancer-related mortality, especially for those patients diagnosed at the locally unresectable or advanced stage, whose survival prognosis is rather pessimistic [2]. Locally unresectable advanced gastric cancer (LAUGC) is characterized by tumor invasion into adjacent critical structures or the presence of distal metastasis, rendering curative complete resection unfeasible [3]. These patients typically experience limited survival and diminished quality of life [4]. Therefore, how to improve the treatment outcome of this patient group, especially through conversion therapy to make the tumor resectable, has become an important topic in current research regarding gastric cancer treatment.

The treatment of LAUGC remains highly challenging. Traditional treatment methods, including chemotherapy, radiotherapy and targeted therapy, have demonstrated limited efficacy due to tumor drug resistance and the complex tumor microenvironment. Moreover, these

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treatments have limited effects in controlling the disease and are often accompanied by severe adverse reactions [5-7]. Although emerging immunotherapies and novel targeted agents have shown promise, their clinical application in gastric cancer is still largely investigational, and the efficacy and drug resistance remain key issues to be urgently solved [8]. Given these limitations, the development of more effective treatment regimens, especially combination regimens integrating chemotherapy and targeted therapy, may become a potential treatment direction.

Among chemotherapeutic agents, paclitaxel, oxaliplatin and fluorouracil are commonly used in clinical practice. Paclitaxel, an anti-microtubule drug, inhibits cell division and induces apoptosis [9]. Oxaliplatin, a platinum-based compound, exerts cytotoxicity by forming DNA cross-links that impair DNA synthesis and repair [10]. Fluorouracil, an antimetabolite, inhibits thymidylate synthase, thereby disrupting DNA replication and repair processes [11]. The combination of these agents in the TPF regimen (paclitaxel, oxaliplatin, and fluorouracil) has shown promising efficacy in gastric cancer [12]. However, its role in conversion therapy for LAUGC has not been well characterized.

This study aimed to investigate the efficacy and safety of the TPF regimen as conversion therapy in patients with LAUGC, with the goal of expanding treatment options and improving clinical outcomes in this difficult-to-treat population.

Methods and materials

Patient selection

This retrospective study included 264 patients with pathologically confirmed LAUGC who were admitted to Lanzhou First People's Hospital between March 2019 and August 2021. Among them, 140 patients who received a combination regimen of paclitaxel, oxaliplatin combined with fluorouracil (TPF) were included in the study group, while 124 patients treated with oxaliplatin combined with fluorouracil (FOLFOX) were included in the control group.

The inclusion criteria were as follows: (1) Histologically confirmed, measurable locally advanced gastric cancer considered suitable for downstaging treatment; (2) Absence of distant metastasis; (3) No significant dysfunction of major organs including the heart, lung, liver, or kidneys; (4) No prior chemotherapy, radiotherapy or surgical intervention; (5) Eastern Cooperative Oncology Group (ECOG) performance status score ≤2; (6) Baseline albumin ≥3.0 g/dL; (7) Availability of complete clinical data.

The exclusion criteria included: (1) Known allergies to paclitaxel, oxaliplatin, calcium folinate or fluorouracil; (2) History of other malignancies within the past 5 years; (3) Active infection or autoimmune disease; (4) Presence of additional malignant tumors; (5) Severe dysfunction of vital organs; (6) Severe myelosuppression; (7) Pregnancy or lactation.

This study obtained the approval of the Medical Ethics Committee of Lanzhou First People's Hospital.

Treatment protocol

Patients receiving the TPF regimen were assigned to the study group. The TPF protocol consisted of paclitaxel (135 mg/m^2; Nanjing Sike Pharmaceutical Co., Ltd., China) administered via intravenous infusion on day 1; oxaliplatin (85 mg/m^2; Jiangsu Aosaikang Pharmaceutical Co., Ltd., China) administered via intravenous infusion on day 1; and fluorouracil (2400 mg/m^2; Tianjin Jinyao Pharmaceutical Co., Ltd., China) delivered as a continuous intravenous infusion over 48 hours (day 1 to day 2). Treatment was administered every 21 days for 4-6 cycles. Patients treated with the FOLFOX regimen were included in the control group. The FOLFOX protocol consisted of oxaliplatin (85 mg/m^2) administered via intravenous infusion on day 1, followed by fluorouracil given as a 400 mg/m^2 intravenous bolus on day 1, and then a 2400 mg/m^2 continuous intravenous infusion over 48 hours (day 1 to day 2). This regimen was repeated every 14 days for 6-8 cycles. Patients who achieved tumor downstaging and met surgical criteria underwent radical gastrectomy with D2 lymphadenectomy.

Data collection and outcome measurements

Demographic characteristics [age, gender, Eastern Cooperative Oncology Group (ECOG) performance status], tumor characteristics

Table 1. General information table

	Control Group (n=124)	Study Group (n=140)	χ^2	P
Age			0.961	0.327
<60 years	47 (37.90)	45 (32.14)		
≥60 years	77 (62.10)	95 (67.89)		
Gender			0.760	0.383
Male	86 (69.35)	90 (64.29)		
Female	38 (30.65)	50 (35.71)		
Histological Differentiation			0.104	0.747
Moderately Differentiated	68 (54.84)	74 (52.86)		
Poorly Differentiated	56 (45.16)	66 (47.14)		
Tumor Diameter			1.204	0.273
<5 cm	51 (41.13)	67 (47.86)		
≥5 cm	73 (58.87)	73 (52.14)		
T Stage			0.457	0.499
T3	72 (58.06)	87 (62.14)		
T4	52 (41.94)	53 (37.86)		
N Stage			0.595	0.743
N1	64 (51.61)	76 (54.29)		
N2	38 (30.65)	44 (31.43)		
N3	22 (17.74)	20 (14.29)		
Lesion Location			0.436	0.804
Antrum	39 (31.45)	39 (27.86)		
Body	36 (29.03)	44 (31.43)		
Cardia	49 (39.52)	57 (40.71)		
Nerve Infiltration			0.202	0.653
Absent	48 (38.71)	58 (41.43)		
Present	76 (61.29)	82 (58.57)		
Family History of Gastric Cancer			0.867	0.352
Present	20 (16.13)	17 (12.14)		
Absent	104 (83.87)	123 (87.86)		
Histological Type			1.007	0.800
Adenocarcinoma	107 (86.29)	122 (87.14)		
Signet Ring Cell Carcinoma	10 (8.06)	8 (5.71)		
Mucinous Adenocarcinoma	5 (4.03)	6 (4.29)		
Undifferentiated Carcinoma	2 (1.61)	4 (2.86)		

T Stage: tumor stage, N Stage: node stage.

(T/N stage, histological differentiation, and lesion location), and baseline laboratory parameters [albumin, lymphocyte count, carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), liver and kidney function] were extracted from electronic medical records. Treatment-related information, including the number of chemotherapy cycles, dose adjustments (defined as >20% reduction from the planned dose), and conversion surgery status (R0 resection is defined as having microscopically negative margins ≥1 mm), was verified through pharmacy administration records and surgical reports. Tumor response was evaluated every two chemotherapy cycles using contrast-enhanced CT or MRI according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. The objective response rate (ORR) was calculated as the sum of complete response (CR) and partial response (PR), while the disease control rate (DCR) included CR, PR, and stable disease [13]. Clinical assess-

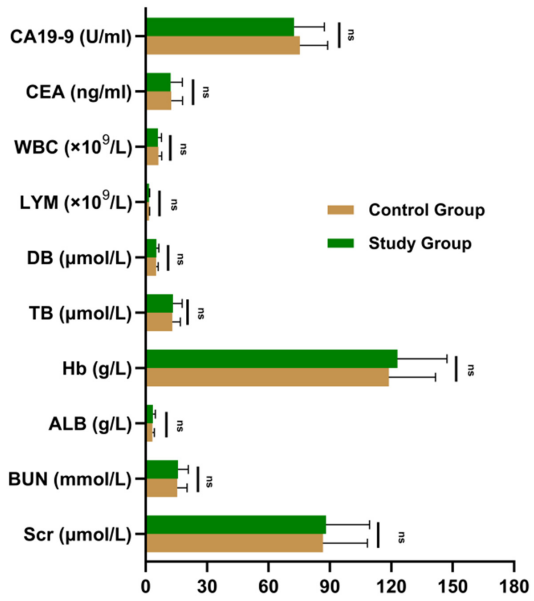

Figure 1. Results of biochemical indicators. Scr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, Hb: hemoglobin, TB: total bilirubin, DB: direct bilirubin, LYM: lymphocyte count, WBC: white blood cell count, CEA: carcinoembryonic antigen, CA19-9: carbohydrate antigen 19-9, Ns: no significant.

ments were conducted weekly during chemotherapy, with toxicity monitoring continued for up to 30 days after treatment completion. Adverse events, including hematological toxicities (e.g., neutropenia, thrombocytopenia) and non - hematological toxicities (e.g., neuropathy, nausea/vomiting), were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 [14]. Survival data were collected through hospital readmission, outpatient visits and telephone follow-up, with a maximum follow-up period of 3 years from the initiation of chemotherapy.

Statistical analysis

All statistical analyses were performed using SPSS 24.0. Measurement data were expressed as mean ± standard deviation, and compared using t-test. Count data were expressed as counts and percentages and analyzed using the chi-square test. Survival outcomes were evaluated using the Kaplan-Meier method, and differences in long-term outcomes between treatment groups were assessed with the log-rank test. Time-dependent ROC curves were generated to assess the prognostic performance of independent factors at specific time points (1-year and 3-year survival), providing insight into the temporal variation of predictive accuracy. A *P*-value less than 0.05 was considered statistically significant.

Results

Baseline clinical characteristics

A comparison of baseline clinicopathological characteristics between the two groups revealed no statistically significant differences in age, gender, histological differentiation, tumor diameter, T stage, N stage, lesion location, perineural infiltration, family history of gastric cancer, or histological subtype (P>0.05), indicating good comparability between groups (**Table 1**).

Baseline biochemical indicators

There were no significant differences between the two groups in terms of baseline serum creatinine (Scr), blood urea nitrogen (BUN), albumin (ALB), hemoglobin (Hb), total bilirubin (TB), direct bilirubin (DB), lymphocyte count (LYM), white blood cell count (WBC), carcinoembryonic antigen (CEA), or carbohydrate antigen 19-9 (CA19-9) levels (P>0.05), as shown in **Figure 1**.

Comparison of treatment efficacy

Following treatment, the ORR rate was significantly higher in the study group (55.71%) compared to the control group (39.84%) (P<0.05). Similarly, the DCR rate was significantly improved in the study group (95.00%) versus the control group (78.05%) (P<0.05), as shown in **Table 2**.

Conversion surgery outcomes

Following treatment, 55 patients in the control group (44.35%) and 84 patients in the study group (60.00%) underwent surgery. The conversion surgery rate was significantly higher in the study group compared to the control group (P<0.05). Additionally, R0 resection was achieved in 47 patients in the control group (37.90%) and 79 patients in the study group (56.43%), also demonstrating a statistically significant difference (P<0.05) (**Table 3**).

Treatment-related adverse events

The most common treatment-related adverse events in both groups included myelosuppres-

Table 2. Treatment efficacy results

	CR	PR	SD	PD	ORR	DCR
Control Group (n=124)	6 (4.84)	43 (34.68)	47 (37.90)	28 (22.58)	49 (39.84)	96 (78.05)
Study Group (n=140)	11 (7.86)	67 (47.86)	55 (39.29)	7 (5.00)	78 (55.71)	133 (95.00)
χ^2					6.61	16.714
P					0.01	<0.001

CR: complete response, PR: partial response, SD: stable disease, PD: progressive disease, ORR: objective response rate, DCR: disease control rate.

Table 3. Results of conversion surgery after treatment

Comparison	Conversion Surgery	R0 Resection
Control Group (n=124)	55 (44.35)	47 (37.90)
Study Group (n=140)	84 (60.00)	79 (56.43)
χ^2	6.458	9.046
P	0.011	0.003

sion, gastrointestinal reactions, hepatic dysfunction, hypertension and renal impairment. Most adverse events were grade 1-2 in severity, with only a small proportion classified as grade 3-4. Symptoms were generally manageable with supportive care, and no treatment-related deaths occurred during the treatment period. While the incidences of gastrointestinal reactions, hepatic dysfunction, hypertension and renal impairment were higher in the study group, the differences were not statistically significant (P>0.05). However, the incidence of myelosuppression was significantly higher in the study group than in the control group (P<0.05) (**Table 4**).

Comparison of prognostic results between the two groups

A comparison of survival outcomes at 1 year and 3 years between the two groups revealed that, in the control group, 52 patients died and 72 patients survived within 1 year, resulting in a 1-year survival rate of 58.06%. In the study group, 42 patients died and 98 patients survived within 1 year, yielding a 1-year survival rate of 70.00%. The 1-year survival rate was significantly higher in the study group compared to the control group (P<0.05). At 3 years, 88 patients in the control group died and 36 patients survived, leading to a 3-year survival rate of 29.03%. In the study group, 90 patients died and 50 patients survived, resulting in a 3-year survival rate of 35.71%. However, no statistically significant difference was observed in the 3-year survival rate between the two groups (P>0.05), as shown in **Figure 2**.

Univariate analysis of prognostic factors

Univariate analysis of 1-year survival revealed significant differences between the survival and death groups in terms of age, histological differentiation, T stage, N stage, ALB, LYM, CEA and treatment method (P<0.05), indicating these factors may influence 1-year survival. For 3-year survival, univariate analysis showed statistically significant differences in age, histological differentiation, T stage, N stage, tumor diameter, ALB, LYM and CEA between the survival and death groups (P<0.05), suggesting these factors may impact the 3-year survival of patients, as shown in **Table 5**.

Multivariate analysis of prognostic factors

Multivariate Cox regression analysis was performed on the factors identified in the univariate analysis. The results showed that a higher N stage, elevated CEA levels, and treatment with FOLFOX were independent risk factors for 1-year mortality of patients (P<0.05), while higher ALB and LYM levels served as independent protective factors (P<0.05). Age, histological differentiation and T stage did not emerge as independent prognostic factors for 1-year survival (P>0.05). For 3-year survival, age ≥60 years, poorly differentiated histology, tumor diameter ≥5 cm, advanced T and N stages, and higher CEA levels were identified as independent risk factors for 3-year mortality (P<0.05), while higher ALB and LYM levels continued to act as independent protective factors (P<0.05) (**Figure 3**).

Predictive value of independent prognostic factors for 1-year survival

Time-dependent ROC curves were constructed to examine the predictive value of independent risk factors for patients' 1-year survival. The

Table 4. Treatment-related adverse events

		Myelosuppression	Gastrointestinal Reactions	Hepatic Dysfunction	Hypertension	Renal Impairment
Control Group (n=124)	Grade 1-2	31 (25.00)	21 (16.94)	14 (11.29)	18 (14.52)	11 (8.87)
	Grade 3-4	12 (9.68)	10 (8.06)	0 (0.00)	6 (4.84)	0 (0.00)
Study Group (n=140)	Grade 1-2	59 (42.14)	30 (21.43)	22 (15.71)	22 (15.71)	22 (15.71)
	Grade 3-4	16 (11.43)	13 (9.29)	0 (0.00)	8 (5.71)	0 (0.00)
χ^2		9.497	1.064	1.093	0.174	2.816
P		0.002	0.302	0.296	0.677	0.093

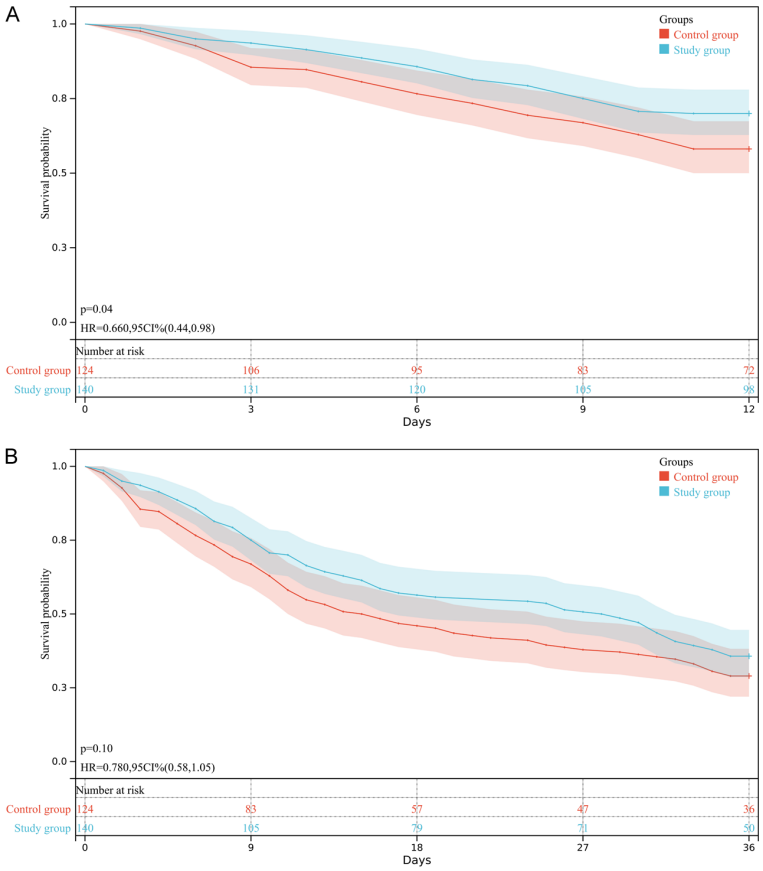

Figure 2. Prognostic outcomes of the two groups. A. Kaplan-Meier curve for 1-year survival. B. Kaplan-Meier curve for 3-year survival.

area under the curve (AUC) for the N stage was 0.650, for ALB was 0.810, for LYM was 0.630, for CEA was 0.700, and for the treatment method was 0.560 (**Figure 4**).

Predictive value of independent prognostic factors for 3-year survival

Time-dependent ROC curves were constructed to assess the predictive value of independent risk factors for patients' 3-year survival. The results revealed the following AUC values: age, 0.600; histological differentiation, 0.580; tumor diameter, 0.590; T stage, 0.600; N stage, 0.620; ALB, 0.700; LYM, 0.620; and CEA, 0.650 (**Figure 5**).

Discussion

This study evaluated the clinical application of the TPF regimen in the conversion therapy of LAUGC. The goal of conversion therapy is to reduce tumor size through effective chemotherapy, thereby making surgical resection feasible and improving long-term survival outcomes [15]. However, patients with advanced gastric cancer often face significant challenges in undergoing radical surgery due to factors such as large tumor burden, complex anatomical location, or poor overall health [16]. Existing studies have shown that multi-drug combination chemotherapy regimens are more effective than single- or double-drug regimens in treating gastric cancer, although their widespread use is often limited by toxic side effects [17]. This study aimed to evaluate whether the TPF regimen can strike an optimal balance between efficacy and safety, providing valuable insights for clinical practice.

The results of this study demonstrate that the TPF regimen achieves superior short-term outcomes in LAUGC conversion therapy, with both ORR and 1-year survival rates significantly high-

Table 5. Univariate analysis of prognostic factors

	1-Year Survival				3-Year Survival			
	Survival Group (n=170)	Death Group (n=94)	χ^2/t	P	Survival Group (n=86)	Death Group (n=178)	χ^2/t	P
Age			11.843	<0.001			9.242	0.002
<60 years	72 (42.35)	20 (21.28)			41 (47.67)	51 (28.65)		
≥60 years	98 (57.65)	74 (78.72)			45 (52.33)	127 (71.35)		
Gender			2.980	0.084			0.034	0.853
Male	107 (62.94)	69 (73.40)			58 (67.44)	118 (66.29)		
Female	63 (37.06)	25 (26.60)			28 (32.56)	60 (33.71)		
Histological Differentiation			6.075	0.014			6.585	0.010
Moderately Differentiated	101 (59.41)	41 (43.62)			56 (65.12)	86 (48.31)		
Poorly Differentiated	69 (40.59)	53 (56.38)			30 (34.88)	92 (51.69)		
Tumor Diameter			1.681	0.195			7.781	0.005
<5 cm	81 (47.65)	37 (39.36)			49 (56.98)	69 (38.76)		
≥5 cm	89 (52.35)	57 (60.64)			37 (43.02)	109 (61.24)		
T Stage			19.036	<0.001			9.039	0.003
T3	119 (70.00)	40 (42.55)			63 (73.26)	96 (53.93)		
T4	51 (30.00)	54 (57.45)			23 (26.74)	82 (46.07)		
N Stage			20.095	<0.001			12.636	<0.001
N1	106 (62.35)	34 (36.17)			59 (68.60)	81 (45.51)		
N2	47 (27.65)	35 (37.23)			19 (22.09)	63 (35.39)		
N3	17 (10.00)	25 (26.60)			8 (9.30)	34 (19.10)		
Lesion Location			2.432	0.296			2.168	0.338
Antrum	47 (27.65)	31 (32.98)			22 (25.58)	56 (31.46)		
Body	57 (33.53)	23 (24.47)			31 (36.05)	49 (27.53)		
Cardia	66 (28.82)	40 (42.55)			33 (38.37)	73 (41.01)		
Nerve Infiltration			0.109	0.742			0.020	0.887
Absent	67 (39.41)	39 (41.49)			34 (39.53)	72 (40.45)		
Present	103 (60.59)	55 (58.51)			52 (60.47)	106 (59.55)		
Family History of Gastric Cancer			0.189	0.664			0.159	0.690
Present	25 (14.71)	12 (12.77)			11 (12.79)	26 (14.61)		
Absent	145 (85.29)	82 (87.23)			75 (87.21)	152 (85.39)		
Histological Type			3.965	0.265			2.560	0.465
Adenocarcinoma	147 (86.47)	84 (89.36)			77 (89.53)	154 (86.52)		
Signet Ring Cell Carcinoma	10 (5.88)	8 (8.51)			3 (3.49)	15 (8.43)		
Mucinous Adenocarcinoma	8 (4.71)	1 (1.06)			3 (3.49)	5 (2.81)		
Undifferentiated Carcinoma	5 (2.94)	1 (1.06)			3 (3.49)	4 (2.25)		
Scr (μmol/L)	87.63±21.76	87.13±21.04	0.181	0.857	85.97±21.49	88.17±21.47	0.780	0.436
BUN (mmol/L)	15.62±5.25	15.73±4.09	0.176	0.861	14.98±5.39	16.00±4.57	1.601	0.111
ALB (g/L)	3.89±0.99	2.71±0.80	9.651	<0.001	3.95±0.93	3.24±1.08	5.230	<0.001
Hb (g/L)	120.43±25.46	122.32±19.78	0.623	0.534	124.69±26.39	119.37±21.95	1.725	0.86
TB (μmol/L)	13.27±4.23	13.13±4.16	0.259	0.796	12.97±4.49	13.35±4.06	0.688	0.492
DB (μmol/L)	5.10±1.23	5.27±1.06	1.128	0.260	5.09±1.10	5.20±1.21	0.713	0.477
LYM ($\times10^9$/L)	1.65±0.35	1.53±0.29	2.830	0.005	1.70±0.35	1.57±0.31	3.060	0.002
WBC ($\times10^9$/L)	6.10±1.61	6.18±1.69	0.380	0.704	6.12±1.43	6.15±1.53	0.153	0.879
CEA (ng/ml)	10.98±5.17	14.93±5.50	5.810	<0.001	10.43±5.25	13.32±5.55	4.035	<0.001
CA19-9 (U/ml)	74.37±14.76	72.93±13.38	0.784	0.434	75.43±15.25	73.10±13.77	1.244	0.215
Treatment			4.086				1.337	0.248
TPF	98 (57.65)	42 (44.68)			50 (58.14)	90 (50.56)		
FOLFOX	72 (42.35)	52 (55.32)			36 (41.86)	88 (49.44)		

T Stage: tumor stage, N Stage: node stage, Scr: serum creatinine, BUN: blood urea nitrogen, ALB: albumin, Hb: hemoglobin, TB: total bilirubin, DB: direct bilirubin, LYM: lymphocyte count, WBC: white blood cell count, CEA: carcinoembryonic antigen, CA19-9: carbohydrate antigen 19-9.

er than those observed with the FOLFOX regimen. These findings align with those of Dai et al. [18], who reported a 52% ORR for TPF in metastatic gastric cancer, highlighting the con-

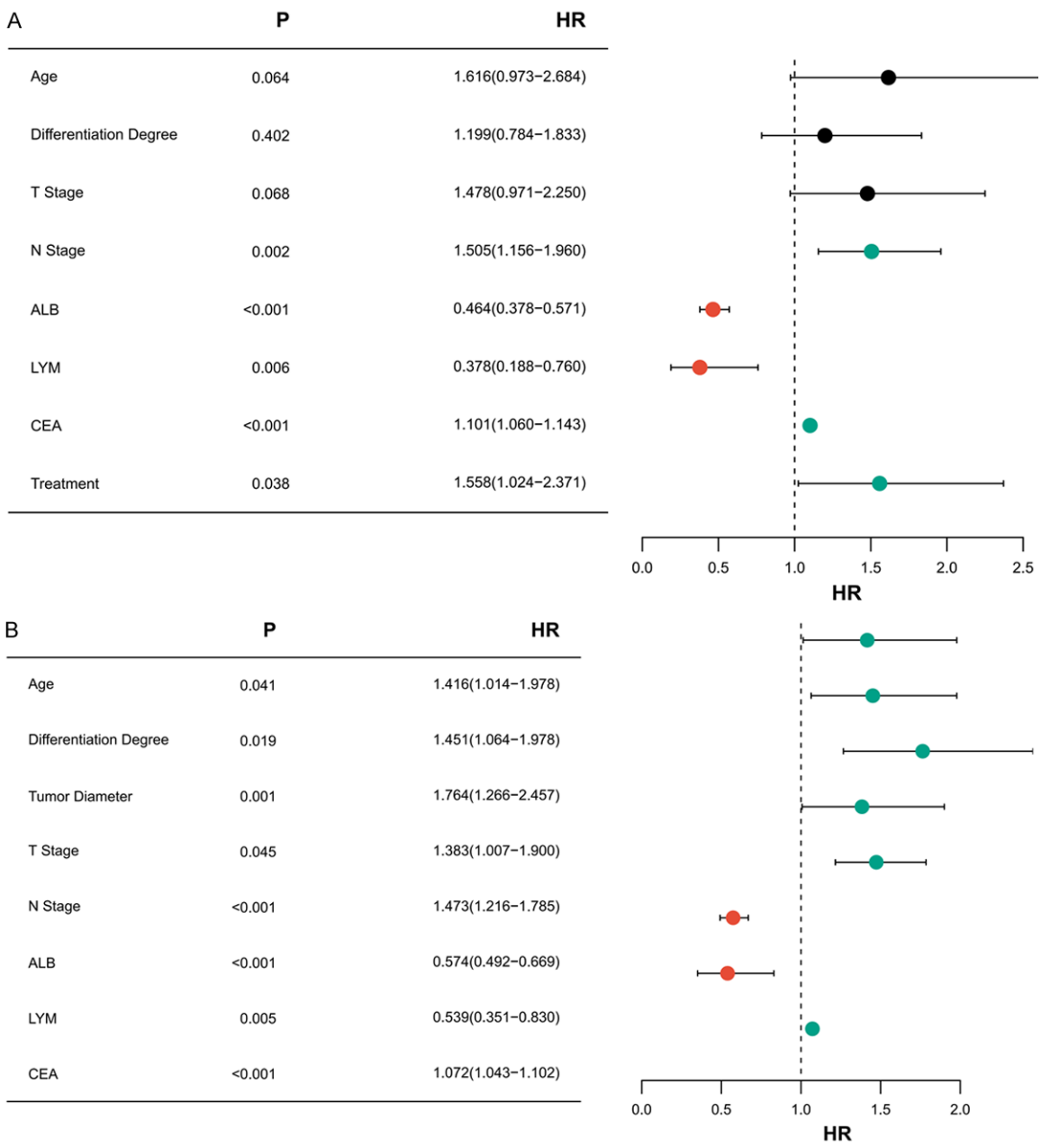

Figure 3. Forest plot of multivariate analysis. A. Forest plot of multivariate analysis for one-year survival prognosis. B. Forest plot of multivariate analysis for three-year survival prognosis. T Stage: Tumor Stage, N Stage: Node Stage, ALB: albumin, LYM: lymphocyte count, CEA: carcinoembryonic antigen.

sistent efficacy across different gastric cancer subtypes. However, the comparable 3-year survival rates between the two regimens mirror the observations of Lan et al. [19], where the initial advantages in response rates diminished over time, possibly due to the development of chemoresistance in residual tumor cells.

The increased myelosuppression observed with the TPF regimen contrasts with the post-operative study by Xie et al. [20], which reported similar toxicity profiles. This discrepancy may reflect the higher pretreatment tumor burden in our cohort. Notably, the grade ≥3 neutropenia rate in our study was lower than that observed in European cohorts [21], which may be attributable to the prophylactic use of growth factors in 68% of our patients - a strategy advocated by Saloustros et al. [21] for taxane-containing regimens. These findings rein-

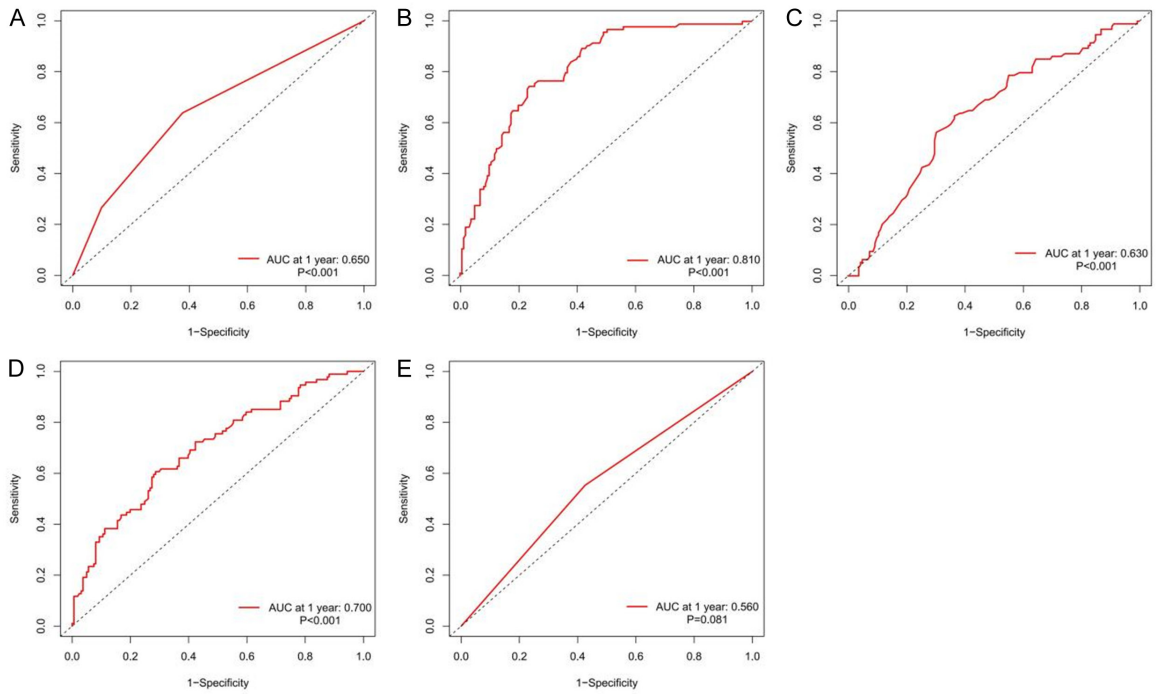

Figure 4. Predictive value of independent influencing factors for 1-year prognosis. A. Time-dependent ROC curve of N stage in predicting patients' 1-year prognosis. B. Time-dependent ROC curve of ALB in predicting patients' 1-year prognosis. C. Time-dependent ROC curve of LYM in predicting patients' 1-year prognosis. D. Time-dependent ROC curve of CEA in predicting patients' 1-year prognosis. E. Time-dependent ROC curve of treatment methods in predicting patients' 1-year prognosis. Note: ROC: receiver operating characteristic, N Stage: node stage, ALB: albumin, LYM: lymphocyte count, CEA: carcinoembryonic antigen.

force that the toxicity profile of the TPF regimen remains manageable through vigilant monitoring. However, elderly patients in our study exhibited a 23% higher treatment interruption rate, which aligns with Kimura et al.'s analyses of surgical risk in this population [22].

Multivariate analysis identified N stage and CEA as persistent risk factors across survival endpoints, supporting the nodal metastasis model proposed by You et al. [23]. The strong prognostic value of ALB (AUC=0.81 at 1 year) reinforces Zhang et al.'s theory on nutritional indices [24], while the predictive power of lymphocyte count aligns with Wang et al.'s hypothesis regarding the role of the immune microenvironment [25]. Interestingly, tumor diameter ≥5 cm showed a lower predictive value for 3-year survival compared to TNM staging, which contrasts with the findings of Cavdar et al. [26]. This discrepancy may be explained by our cohort's exclusion of patients with distant metastases.

This study provides new evidence supporting the treatment of LAUGC. The TPF regimen shows promising efficacy in conversion therapy and is expected to become a viable treatment option, offering hope for improving the prognosis of patients. However, as a retrospective study, it is subject to potential selection biases. Future prospective, multi-center, large-sample randomized controlled trials are needed to more accurately evaluate the efficacy and safety of the TPF regimen in LAUGC conversion therapy. Additionally, in-depth research is needed to explore strategies for minimizing, toxicity and side effects while improving patients' quality of life, ultimately providing a more robust scientific basis for the individualized treatment of LAUGC patients.

In conclusion, the TPF regimen exhibits strong efficacy in the conversion therapy of LAUGC, with manageable myelosuppression and a notable advantage in 1-year survival. The identification of related risk factors provides valuable insights for clinical decision-making.

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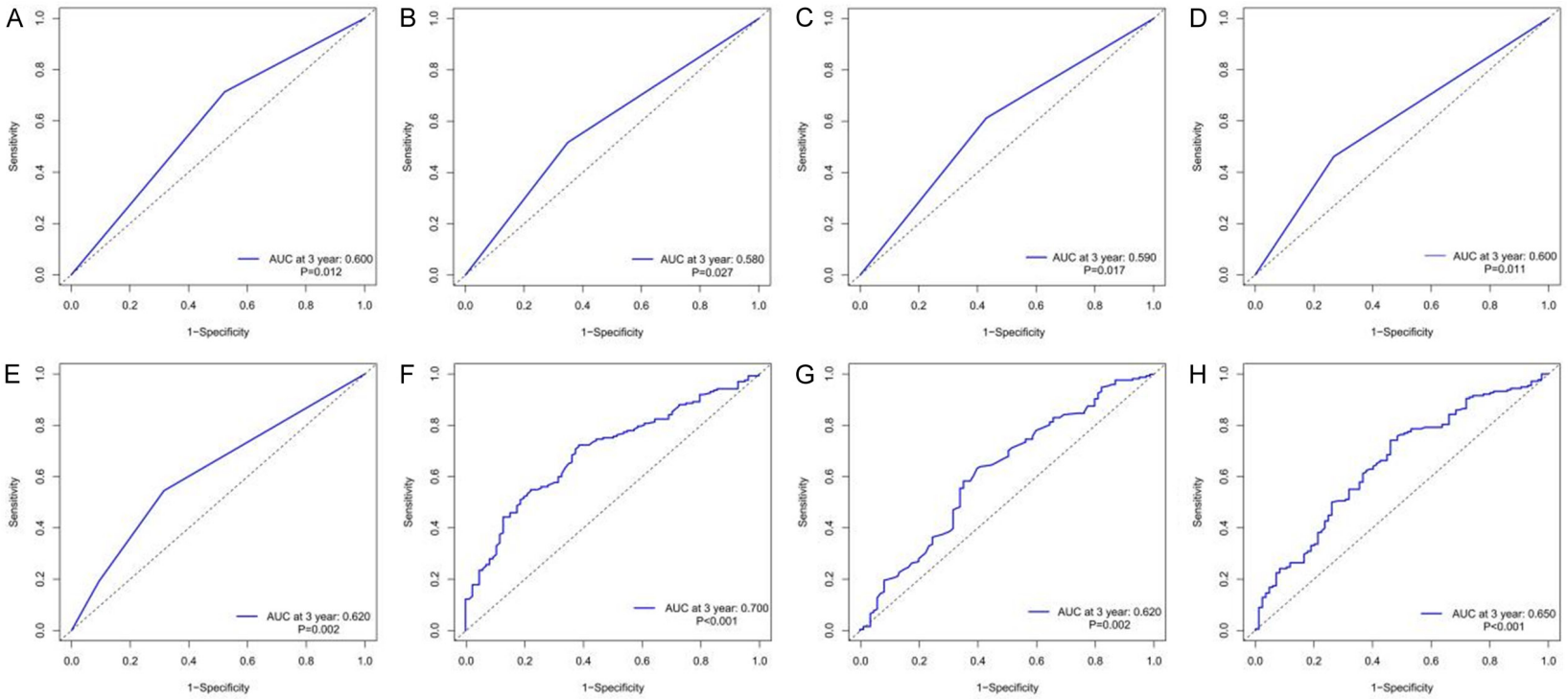

Figure 5. Predictive value of independent influencing factors for 3-year prognosis. A. Time-dependent ROC curve of age in predicting patients' 3-year prognosis. B. Time-dependent ROC curve of the degree of differentiation in predicting patients' 3-year prognosis. C. Time-dependent ROC curve of tumor diameter in predicting patients' 3-year prognosis. D. Time-dependent ROC curve of T stage in predicting patients' 3-year prognosis. E. Time-dependent ROC curve of N stage in predicting patients' 3-year prognosis. F. Time-dependent ROC curve of ALB in predicting patients' 3-year prognosis. G. Time-dependent ROC curve of LYM in predicting patients' 3-year prognosis. H. Time-dependent ROC curve of CEA in predicting patients' 3-year prognosis. Note: ROC: receiver operating characteristic, T Stage: tumor stage, N Stage: node stage, ALB: albumin, LYM: lymphocyte count, CEA: carcinoembryonic antigen.

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Disclosure of conflict of interest

None.

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