Pretreatment C-reactive protein-triglyceride-glucose index predicts survival in patients with FLOT-treated locally advanced gastric and gastroesophageal junction cancer

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Received January 14, 2026; Accepted March 20, 2026

DOI: 10.3892/ol.2026.15585

Abstract. The C-reactive protein-triglyceride-glucose index (CTI), integrating C-reactive protein and the triglyceride-glucose index, is a pragmatic biomarker reflecting systemic inflammation and metabolic stress in cancer. Although its prognostic value has been validated in heterogeneous cancer cohorts, data in homogeneous perioperative settings remain limited. The present study retrospectively evaluated 131 patients with locally advanced gastric or gastroesophageal junction adenocarcinoma who received perioperative fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) chemotherapy between November 2018 and June 2024 (67 months). CTI was calculated at diagnosis, and patients were stratified using the 4.78 cut-off value previously validated in oncology populations. Associations between CTI and clinicopathological variables, pathological response, progression-free survival (PFS) and overall survival (OS) were analyzed. The results demonstrated that among the 131 patients who underwent curative-intent surgery after neoadjuvant FLOT, 113 (86.3%) had low CTI (<4.78) and 18 (13.7%) had high CTI (≥4.78). Patients with high CTI had significantly shorter PFS compared with those with low CTI (median, 12.2 vs. 25.5 months; P=0.006). OS was also markedly inferior in the high CTI group [median, 23.1 months vs. not reached (NR) in the low CTI group; P=0.001]. In the multivariable analysis, high CTI independently predicted poor PFS [hazard ratio (HR), 2.18; 95% confidence interval (CI), 1.21-3.95; P=0.010]. Regarding treatment response, the pathological complete response rate was 11.5% (13/113) in the low CTI group and 22.2% (4/18) in the high CTI group (P=0.221), indicating no significant association between CTI and pathological complete response. In conclusion, pretreatment CTI is an independent prognostic marker in patients with locally advanced gastric or gastroesophageal junction adenocarcinoma treated with perioperative FLOT, identifying individuals at higher risk of relapse and inferior survival. The simplicity, low cost and pretherapeutic availability of pretreatment CTI support its use as a promising tool for risk stratification that warrants prospective, multicenter validation.

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Key words: C-reactive protein-triglyceride-glucose index, gastric cancer, gastroesophageal junction cancer, FLOT, prognosis, survival

Introduction

Gastric and gastroesophageal junction (GEJ) adenocarcinomas remain a major cause of cancer-related mortality worldwide. Despite advances in multimodal strategies combining perioperative chemotherapy and surgery, long-term survival outcomes for locally advanced disease remain unsatisfactory. The fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT) regimen has been established as the standard perioperative treatment subsequent to a survival advantage being demonstrated in randomized trials (1-3). Nevertheless, pathological complete response (pCR) rates after neoadjuvant FLOT remain low, typically ranging from 4 to 20%, underlining the need for reliable biomarkers that can identify patients most likely to benefit (2).

Cancer cachexia and systemic inflammation are common in gastric malignancies and have been consistently associated with a poor prognosis (3,4). Although sarcopenia has been associated with outcomes in certain FLOT-treated cohorts, its assessment requires specialized imaging and time-consuming measurements, limiting routine clinical applicability (5). This has created growing interest in simple, reproducible biomarkers derived from standard laboratory parameters.

The C-reactive protein (CRP)-triglyceride-glucose (TyG) index (CTI), which integrates CRP with the TyG index, reflects both inflammatory and metabolic alterations. The index was originally developed and validated by Ruan *et al* (6) across heterogeneous cancer populations and has subsequently been evaluated in different clinical settings, including advanced-stage disease, metastatic cohorts and non-surgical populations. More recently, Uyar *et al* (7) suggested that

a threshold (4.78, unitless) may have particular prognostic relevance in patients with cancer.

Therefore, the present study aimed to investigate the prognostic value of pretreatment CTI in a homogeneous cohort of patients with locally advanced gastric and GEJ adenocarcinoma treated with perioperative FLOT. To the best of our knowledge, this is the first study applying CTI in this specific setting, thereby serving as an external validation in a clinically important population.

Patients and methods

Study design and patient selection. The present retrospective cohort study was performed at the Department of Internal Medicine and Medical Oncology, Erzurum City Hospital (Erzurum, Türkiye) and included patients diagnosed with locally advanced gastric or GEJ adenocarcinoma who received neoadjuvant chemotherapy with the FLOT regimen followed by surgical resection between November 2018 and June 2024 (67 months). Ethical approval for the study was obtained from the Erzurum Health Sciences University Ethics Committee, the institutional ethics board overseeing Erzurum City Hospital (Erzurum, Turkiye; approval no. 66). Owing to the retrospective design, the requirement for informed consent was waived.

Only patients who underwent surgical resection after completing neoadjuvant chemotherapy and had available data for pathological response assessment were included. Patients were excluded if they had metastatic disease at diagnosis, were lost to follow-up during treatment, received non-FLOT neoadjuvant regimens or had incomplete laboratory data. Specifically, patients lacking sufficient laboratory parameters to calculate the CTI, such as serum triglyceride, glucose or CRP levels at diagnosis, were excluded from the final analysis.

All patients received at least four cycles of standard FLOT chemotherapy, consisting of docetaxel (50 mg/m^2), oxaliplatin (85 mg/m^2), leucovorin (200 mg/m^2) and 5-fluorouracil (2,600 mg/m^2) (24-h infusion) administered every 14 days. Surgery was performed following completion of neoadjuvant therapy in patients deemed resectable, and resection specimens were evaluated by pathologists for histopathological response. Demographic and clinical data collected included age, sex, body mass index, tumor location (gastric vs. GEJ), clinical Tumor-Node-Metastasis (TNM) stage (AJCC 8th edition) (8), Eastern Cooperative Oncology Group performance status (9), HER2 and microsatellite instability (MSI) status, and baseline hemoglobin, albumin, CRP, triglyceride and fasting glucose levels. CTI, a composite score reflecting systemic inflammation and metabolic dysregulation, was calculated using the following formula (6): CTI=0.412 x ln(CRP) + TyG index. The TyG index was defined as: TyG index=ln[triglyceride (mg/dl) x glucose (mg/dl)/2] (6).

Patients were stratified into two groups using a cut-off value of 4.78 (unitless), as reported by Uyar *et al* (7) in a recent validation study of patients with cancer. This lower threshold was preferred over the higher cut-off value of 5.20 proposed by Ruan *et al* (6) in heterogeneous cancer cohorts, as it has been reported to better reflect outcomes in clinical oncology populations.

Pathological tumor response was assessed using the modified Ryan Tumor Regression Grade (TRG) system (10), as recommended by the College of American Pathologists protocol for gastric carcinoma (version 4.2.0.0; 2022). TRG scores were categorized as follows: TRG 0, complete response; TRG 1, moderate response; TRG 2, minimal response; and TRG 3, poor or no response. For subgroup analysis, patients with TRG 0-1 were considered good responders, whilst those with TRG 2-3 were considered poor responders. pCR was defined as the absence of residual tumor cells in the resected specimen (TRG 0).

Progression-free survival (PFS) was defined as the time from diagnosis to radiologically confirmed progression or death from any cause. Overall survival (OS) was defined as the time from diagnosis to death from any cause or last follow-up.

Statistical analysis. All statistical analyses were performed using SPSS version 25.0 (IBM Corp.). Descriptive statistics are expressed as means, medians, standard deviations and percentages. Categorical variables, including sex, tumor location, TNM stage, HER2 status, MSI status and CTI group comparisons, were analyzed using the χ^2 test or Fisher's exact test as appropriate. Fisher's exact test was applied when the assumptions of the χ^2 test were not met (expected cell counts <5). Continuous variables between groups were compared using the independent samples t-test or Mann-Whitney U-test based on data distribution. Kaplan-Meier survival analysis was used to estimate PFS and OS, and differences between groups were evaluated using the log-rank test. Cox proportional hazards regression was used for multivariate analysis; variables with P<0.10 in the univariate analysis were included. Based on univariate screening, clinical stage and CTI were included in the final multivariable model. The proportional hazards assumption was tested using Schoenfeld residuals. Missing laboratory data were handled by complete-case analysis. P<0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics. A total of 146 patients with locally advanced gastric or GEJ adenocarcinoma who received neoadjuvant FLOT chemotherapy followed by curative-intent surgery were included in the present study. The median age of the study population was 62 (IQR, 54-67) years, and 57.5% were men. At diagnosis, 83.6% of the patients had stage II disease, whilst 16.4% had stage III disease. Regarding tumor location, 86.3% had gastric tumors and 13.7% had GEJ tumors. HER2 positivity was detected in 8.2% of patients, and only 1 patient (0.7%) had MSI-high status. The baseline demographic and clinical characteristics of the patients are summarized in Table I.

Association between CTI and clinicopathological features. Patients were stratified into two groups according to the CTI score (<4.78 vs. ≥4.78), and a comparative analysis was performed. The associations between preoperative CTI score and demographic and clinical parameters are presented in Table I. No statistically significant differences were observed between the CTI groups in terms of age, sex, tumor location,

Table I. Baseline demographic and clinical characteristics of the study population and comparison according to the CTI score (n=146).

Characteristic	Total	CTI score		P-value
		Low (<4.78)	High (≥4.78)	
Age, years				0.107
<65	94 (64.4)	84 (67.2)	10 (47.6)	
≥65	52 (35.6)	41 (32.8)	11 (52.4)	
Sex				0.931
Female	62 (42.5)	54 (43.2)	8 (38.1)	
Male	84 (57.5)	71 (56.8)	13 (61.9)	
Location				0.277
GEJ	20 (13.7)	19 (15.2)	1 (4.8)	
Gastric	126 (86.3)	106 (84.8)	20 (95.2)	
TNM stage				0.144
II	122 (83.6)	106 (84.8)	16 (76.2)	
III	24 (16.4)	19 (15.2)	5 (23.8)	
IV	0 (0)	0 (0)	0 (0)	
HER2 status				0.011
Negative	134 (91.8)	118 (94.4)	16 (76.2)	
Positive	12 (8.2)	7 (5.6)	5 (23.8)	
MSI status				0.796
MSS	22 (15.1)	20 (16)	2 (9.5)	
MSI	1 (0.7)	1 (0.8)	0 (0)	
Unknown	123 (84.2)	104 (83.2)	19 (90.5)	
Surgical status				0.678
Yes	131 (89.7)	113 (90.4)	18 (85.7)	
No (progression)	15 (10.3)	12 (9.6)	3 (14.3)	

Values are expressed as n (%). CTI, C-reactive protein-triglyceride-glucose index; GEJ, gastric and gastroesophageal junction; TNM, Tumor-Node-Metastasis; MSI, microsatellite instability; MSS, microsatellite stable.

TNM stage, MSI status or surgical intervention (all P>0.05). However, HER2 positivity was significantly more frequent in patients with high CTI scores compared with those with low CTI scores (23.8 vs. 5.6%; P=0.011). Similarly, the pCR rate did not differ significantly between the CTI groups (P=0.464; Table II).

Although 146 patients received neoadjuvant FLOT chemotherapy, only 131 underwent curative-intent surgery and were included in the final analysis of pathological response and survival outcomes. A total of 15 patients exhibited disease progression during post-chemotherapy response evaluation and therefore did not undergo surgery. Consequently, statistical comparisons and outcome analyses were limited to the surgical cohort. The patient selection process is summarized in Fig. 1.

Pathological response analysis. A pCR was observed in 17 patients (13.0%). Among the 111 patients in the low CTI group, 13 (11.7%) achieved a pCR, whilst 4/18 patients (22.2%) in the high CTI group achieved a pCR (P=0.221). The clinical characteristics of patients with and without pCR are summarized in Table II. When stratified by demographic and clinicopathological variables, there were no statistically significant differences in pCR rates according to sex (P=0.745), tumor location (P=0.456), TNM stage (P=0.588), HER2 status (P=0.602) or MSI status (P=0.455). Although the P-value for age did not reach statistical significance (P=0.068), a numerically higher pCR rate was observed in patients aged ≥65 years (58.8%) compared with those aged <65 years (41.2%).

TRG data are presented in Table III. Among the 131 patients who underwent curative-intent surgery, only 42 (32%) demonstrated a good pathological response (TRG 0-1). The good TRG (0-1) response rate was 44.4% (8/18) in the high CTI group, whilst it was 30.1% (34/113) in the low CTI group (P=0.225). There were no statistically significant differences in TRG response according to age (P=0.448), sex (P=0.515), tumor location (P=0.438), TNM stage (P=0.377), HER2 status (P=0.582) or MSI status (P=0.155).

Survival analysis. The median PFS for the entire cohort was 27.4 months. There were no significant differences in PFS according to age, sex, tumor location, HER2 status or MSI

Table II. Demographic and clinical characteristics stratified by pCR status.

Characteristic	pCR status		P-value
	No pCR	pCR	
Age, years			0.068
<65	72 (64.3)	7 (41.2)	
≥65	40 (35.7)	10 (58.8)	
Sex			0.745
Female	49 (43.8)	7 (41.2)	
Male	63 (56.3)	10 (58.8)	
Location			0.456
GEJ	16 (14.3)	1 (5.9)	
Gastric	96 (85.7)	16 (94.1)	
TNM stage			0.588
II	93 (83.0)	15 (88.2)	
III	19 (17.0)	2 (11.8)	
HER2 status			0.602
Negative	101 (90.2)	16 (94.1)	
Positive	11 (9.8)	1 (5.9)	
MSI status			0.455
MSS	18 (16.1)	2 (11.8)	
MSI	1 (0.9)	0 (0)	
Unknown	93 (83.0)	15 (88.2)	
CTI score			0.221
<4.78	98 (87.5)	13 (76.5)	
≥4.78	14 (12.5)	4 (23.5)	

Values are expressed as n (%). CTI, C-reactive protein-triglyceride-glucose index; TNM, Tumor-Node-Metastasis; MSI, microsatellite instability; MSS, microsatellite stable; pCR, pathological complete response.

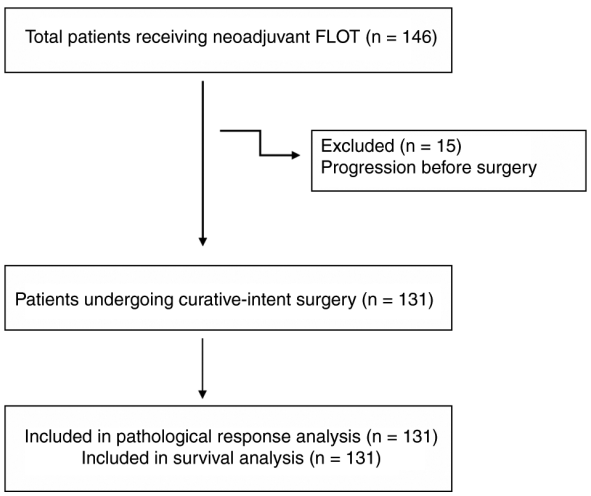

Figure 1. Patient flow diagram. A total of 146 patients received neoadjuvant FLOT chemotherapy. A total of 15 patients experienced disease progression before surgery and were excluded. The remaining 131 patients underwent curative-intent surgery and were included in analyses of pathological response and survival outcomes. FLOT, fluorouracil, leucovorin, oxaliplatin and docetaxel.

Table III. Distribution of clinical and pathological features according to the pathological TRG response.

Characteristic	TRG		P-value
	Poor response (2-3)	Good response (0-1)	
Age, years			0.448
<65	57 (64.0)	24 (57.1)	
≥65	32 (36.0)	18 (42.9)	
Sex			0.515
Female	37 (41.6)	20 (47.6)	
Male	52 (58.4)	22 (52.4)	
Location			0.438
GEJ	17 (19.1)	1 (2.4)	
Gastric	72 (80.9)	41 (97.6)	
TNM stage			0.377
II	73 (82.0)	37 (88.1)	
III	16 (18.0)	5 (11.9)	
HER2 status			0.582
Negative	80 (89.9)	39 (92.9)	
Positive	9 (10.1)	3 (7.1)	
MSI status			0.155
MSS	17 (19.1)	3 (7.1)	
MSI	1 (1.1)	0 (0)	
Unknown	71 (79.8)	39 (92.9)	
CTI score			0.225
<4.78	79 (88.8)	34 (81)	
≥4.78	10 (11.2)	8 (19)	

Values are expressed as n (%). TRG was assessed using the modified Ryan system. TRG 0-1 was defined as a good pathological response, whilst TRG 2-3 was defined as a poor response. TRG, tumor regression grade; CTI, C-reactive protein-triglyceride-glucose index; TNM, Tumor-Node-Metastasis; MSI, microsatellite instability; MSS, microsatellite stable.

status. However, patients with stage II disease had a significantly longer median PFS time compared with those with stage III disease (31.4 vs. 17.3 months; P=0.037). By contrast, no statistically significant difference in PFS was demonstrated between patients with and without pCR (P=0.477). When stratified by CTI score, a significant difference in PFS was observed between the low-risk (CTI <4.78) and high-risk (CTI ≥4.78) groups. The median PFS was 25.5 months in the low CTI group, compared with only 12.2 months in the high CTI group (P=0.006) (Fig. 2). In the multivariate Cox regression analysis, a high CTI score remained an independent predictor of poor PFS (hazard ratio, 2.18; 95% CI, 1.21-3.95; P=0.01).

For the entire cohort, the median OS time was not reached, with a mean OS time of 52.6 months (95% CI, 45.3-59.9). There were no significant differences in OS according to age, sex, tumor location, clinical stage, HER2 status, MSI status, TRG score or pCR. However, patients with a high CTI score

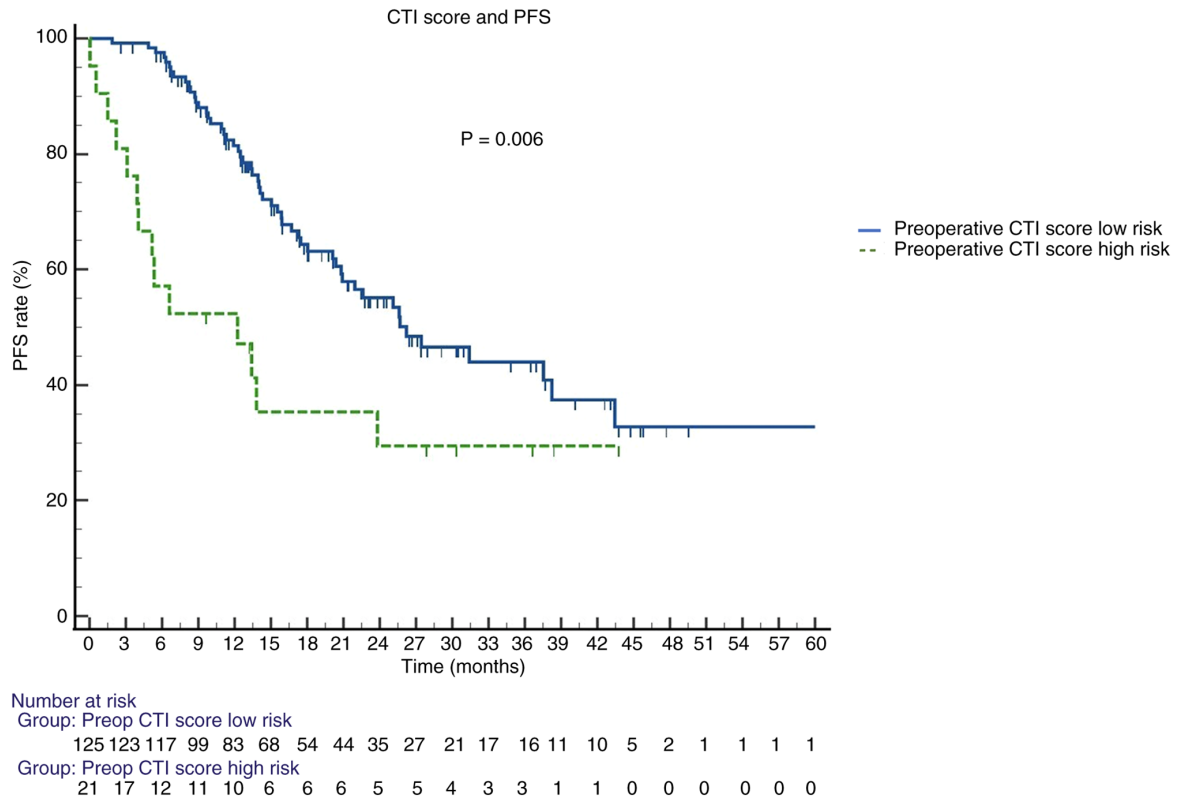

Figure 2. Kaplan-Meier curves for PFS according to CTI groups. PFS time was significantly shorter in patients with high CTI scores (≥4.78) compared with that in patients with low CTI scores (<4.78) (hazard ratio, 2.18; 95% confidence interval, 1.21-3.95; P=0.006, log-rank test). PFS, progression-free survival; CTI, C-reactive protein-triglyceride-glucose index.

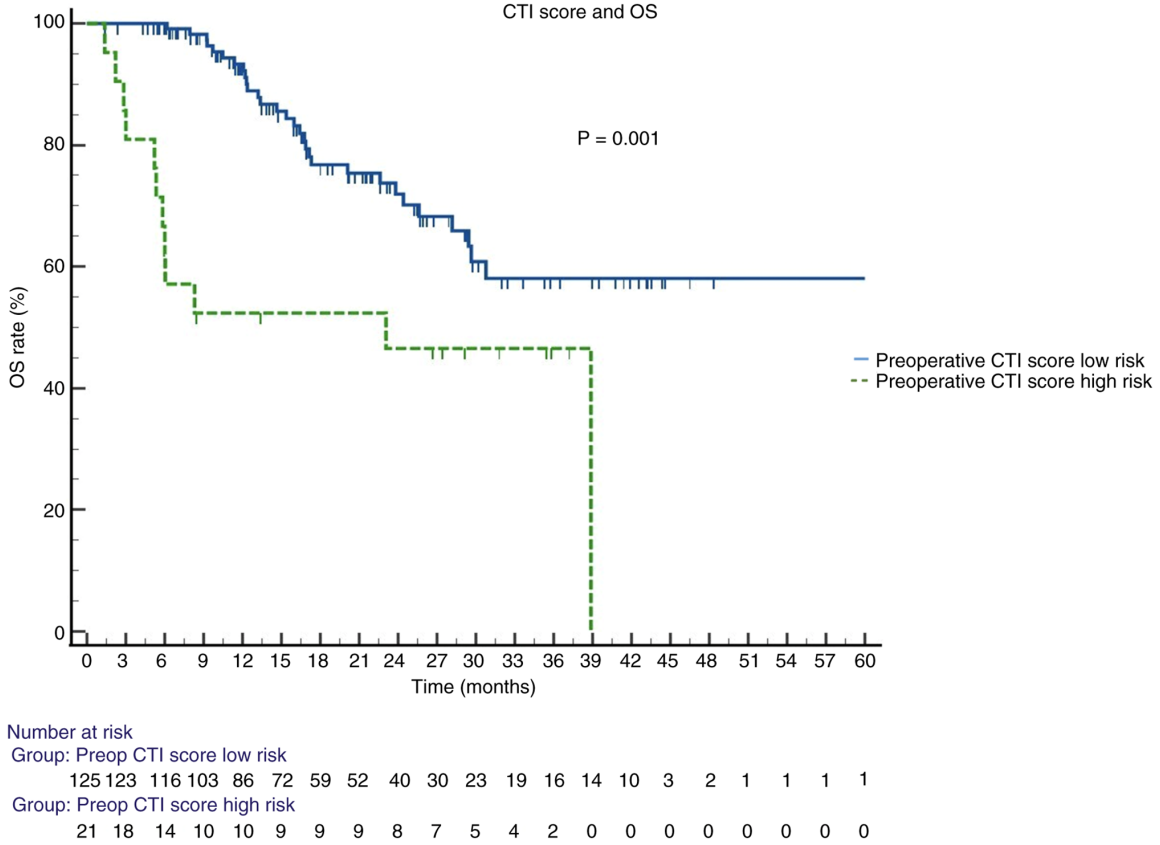

Figure 3. Kaplan-Meier curves for OS according to CTI groups. OS time was significantly shorter in patients with high CTI scores (≥4.78) compared with that in patients with low CTI scores (<4.78) (hazard ratio, 2.45; 95% confidence interval, 1.39-4.32; P=0.001, log-rank test). OS, overall survival; CTI, C-reactive protein-triglyceride-glucose index.

Table IV. Survival analysis results (log-rank test).

Variable	PFS P-value	OS P-value
Age (≥65 vs. <65 years)	0.936	0.292
Sex (male vs. female)	0.128	0.343
Tumor location (GEJ vs. gastric)	0.982	0.726
Clinical stage (III vs. II)	0.037	0.377
HER2 status (positive vs. negative)	0.784	0.443
MSI status (MSI vs. MSS/unknown)	0.545	0.475
TRG (0-1 vs. 2-3)	0.115	0.263
Pathological complete response	0.477	0.599
CTI (≥4.78 vs. <4.78)	0.006	0.001

PFS and OS were analyzed using the Kaplan-Meier method and compared using the log-rank test. PFS, progression-free survival; OS, overall survival; GEJ, gastric and gastroesophageal junction; TNM, Tumor-Node-Metastasis; MSI, microsatellite instability; MSS, microsatellite stable; TRG, tumor regression grade; CTI, C-reactive protein-triglyceride-glucose index.

had a significantly shorter median OS of 23.1 months (95% CI, 10.52-35.60), whereas the median OS was not reached in the low CTI group (P=0.001; log-rank test) (Fig. 3). The results of the Kaplan-Meier survival analyses for all evaluated clinicopathological variables are summarized in Table IV. The results of the multivariable Cox regression analysis for OS are presented in Table V.

Table V. Multivariable Cox regression analysis for overall survival.

Variable	HR (95% CI)	P-value
Clinical stage (III vs. II)	1.43 (0.65-3.12)	0.377
CTI (≥4.78 vs. <4.78)	2.45 (1.39-4.32)	0.002

HR, hazard ratio; CI, confidence interval.

Discussion

The results of the present study demonstrated that a higher pretreatment CTI score was significantly associated with worse PFS and OS times in patients with locally advanced gastric or GEJ adenocarcinoma treated with perioperative FLOT. By contrast, there was no association between CTI and pCR or TRG, indicating that it primarily reflects host-related biological vulnerability rather than tumor chemosensitivity. The findings suggest that baseline systemic inflammation and metabolic dysregulation captured by CTI may define a subset of patients at elevated risk of early relapse despite standard multimodality therapy. In addition, pCR did not translate into a survival advantage in the present cohort. This unexpected finding may partly be explained by the limited number of pCR cases and, consequently, the restricted statistical power. This suggests that survival outcomes in this population may be driven more strongly by host-related systemic factors than by pathological response alone.

Despite recent advances in perioperative chemotherapy and surgical standardization, long-term outcomes for locally advanced GEJ cancers remain suboptimal, with relapse rates approaching 40-50% even after curative-intent treatment (11,12). The FLOT regimen has improved pathological response and survival rates compared with earlier perioperative protocols, yet a substantial proportion of patients still experience early progression or recurrence, reflecting profound biological heterogeneity (1,11). As underscored in recent studies evaluating systemic host factors, such as the prognostic nutritional index (PNI) and perioperative sarcopenia-related muscle loss, nutritional and inflammatory derangements critically influence treatment tolerance and outcomes in gastric cancer (13,14). However, most existing prognostic tools remain tumor-centric and rely on postoperative variables (such as pathological stage, lymphovascular invasion or surgical complications), limiting their applicability before treatment initiation (15). In this regard, CTI, derived from routine laboratory parameters integrating systemic inflammation and metabolic dysfunction, provides a readily measurable pretherapeutic marker. Unlike indices such as PNI, which may fluctuate with transient hematological or procedural factors, or sarcopenia assessment requiring dedicated imaging and software, CTI offers a stable, objective and easily obtainable metric, enabling consistent and reproducible risk stratification even in resource-limited clinical settings.

The results of the present study are consistent with growing evidence that metabolic and inflammatory pathways critically shape therapeutic outcomes in gastric cancer. Prior studies have reported that host-related indices reflecting systemic inflammation, such as PNI and sarcopenia, are strongly associated with survival (16,17). The present findings extend these observations by demonstrating that CTI, representing both inflammatory burden and metabolic stress, serves as an independent prognostic indicator even in a uniform FLOT-treated population. As CTI combines CRP, reflecting systemic inflammation, and the TyG index, representing insulin resistance (6), higher CTI values may indicate a biological environment characterized by persistent inflammatory and metabolic disturbances that contribute to tumor progression and worse survival outcomes.

Mechanistically, elevated CTI likely captures a state of chronic low-grade inflammation and insulin resistance that synergistically fosters tumor progression. Experimental and clinical studies have reported that chemotherapy itself can exacerbate systemic inflammation through activation of NF-κB, STAT3 and IL-6 signaling, leading to angiogenesis, epithelial-mesenchymal transition and metastasis (17). Similarly, metabolic perturbations typical of insulin-resistant or obese states enhance mTOR and PI3K/AKT signaling, impair cytotoxic T-cell function and impair chemotherapy response (17,18). Together, these findings provide a plausible explanation for the strong prognostic impact of CTI on survival but not on pathological response. Whilst tumor

chemosensitivity is largely treatment-dependent, systemic inflammation and metabolic dysregulation act as persistent host-level modifiers that influence recurrence and OS trajectories. Consistent with this interpretation, in the present study, patients with higher CTI values showed numerically higher rates of good pathological tumor regression, yet experienced inferior survival outcomes, further supporting the hypothesis that systemic host vulnerability rather than tumor chemosensitivity predominantly influences long-term prognosis. In addition, HER2 positivity was more frequent among patients with elevated CTI values. Although the biological basis of this association remains unclear, it may suggest a potential interaction between tumor biology and systemic inflammatory-metabolic status, warranting further evaluation in future studies.

The clinical relevance of CTI has recently been reinforced by large-scale prospective and validation studies across heterogeneous cancer populations. Ruan *et al* (6) demonstrated in >1,700 patients with cancer cachexia that higher CTI values independently predicted both short- and long-term mortality across multiple tumor types. In parallel, Uyar *et al* (7) externally validated CTI within the PROMISE-CTI Combined Score, reporting notable discriminatory accuracy for 90-day mortality among hospitalized patients with cancer. Together, these data establish CTI as a reproducible inflammation- and metabolism-based biomarker with prognostic value beyond specific tumor contexts. The findings of the present study further demonstrate the prognostic significance of CTI in a homogeneous, perioperative FLOT-treated gastric cancer cohort. Integrating these results suggests that CTI could serve as a unifying biomarker bridging advanced stage and potentially curative settings. Given the mounting evidence, future prospective multicenter trials directly comparing CTI with established nutritional and inflammatory indices in defined treatment cohorts are warranted to validate its clinical utility and to determine whether targeted modulation of CTI through anti-inflammatory or metabolic interventions can translate into improved oncological outcomes.

The present study has several strengths. All patients were treated with a uniform perioperative FLOT protocol at a tertiary referral center, minimizing treatment-related heterogeneity. CTI was assessed pre-therapeutically using readily available laboratory parameters, allowing unbiased evaluation of its prognostic relevance before any chemotherapy-induced metabolic or inflammatory alterations. Moreover, the analysis in the present study provides one of the first disease-specific validations of CTI within a curative-intent gastric cancer cohort, to the best of our knowledge, bridging the evidence previously derived from advanced or cachectic populations. Nonetheless, several limitations should be acknowledged. The retrospective and single-center design may introduce selection bias, and the relatively small number of patients in the high CTI score subgroup limits statistical power for pathological response analyses. Moreover, baseline metabolic confounders, such as diabetes, dyslipidemia or use of corticosteroids, could not be fully adjusted for. In addition, dynamic changes in CTI during treatment and their association with survival were not assessed. Another limitation is the lack of external multicenter validation, as the findings were derived from a single institutional cohort. Furthermore, comorbid metabolic conditions and concomitant medications may have influenced CTI values and survival outcomes but could not be comprehensively controlled for in the retrospective analysis. These factors should be addressed in future prospective multicenter studies with longitudinal biomarker monitoring.

In conclusion, the findings of the present study demonstrate that pretreatment CTI independently predicts PFS and OS time in patients with locally advanced gastric or GEJ adenocarcinoma undergoing perioperative FLOT therapy, without an association with pathological response. Together with emerging multicancer and hospital-based evidence, the results support CTI as a robust, inexpensive and easily implementable prognostic tool in oncology. However, prospective validation and interventional trials targeting systemic inflammation and metabolic dysregulation are warranted to determine whether modulating CTI can translate into tangible survival benefit.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

AD conceived and designed the study, performed the data analysis and drafted the manuscript. MT contributed to the surgical data interpretation and critically revised the manuscript for important intellectual content. OS supervised the study, contributed to study design and data interpretation, and critically revised the manuscript for important intellectual content and performed the final manuscript review. All authors have read and approved the final manuscript. AD, MT and OS confirm the authenticity of all the raw data.

Ethics approval and consent to participate

This study was approved by the Erzurum Health Sciences University Ethics Committee (Erzurum, Türkiye; approval no. 66). Due to the retrospective nature of the study, the requirement for informed consent was waived. All procedures were conducted in accordance with the ethical standards of the institutional ethics committee and the Declaration of Helsinki.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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