# Efficacy of the Combination of Modified Docetaxel, Cisplatin and Fluorouracil in Locally Advanced Gastric Cancer: Evaluation of Real-Life Outcomes

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**ABSTRACT**

Our study aimed to evaluate the efficacy and demonstrate the real-life outcomes of the combination of modified Docetaxel, Cisplatin, and Fluorouracil (mDCF) as perioperative chemotherapy in patients with locally advanced gastric cancer. The study included 151 patients diagnosed with locally advanced gastric cancer. Modified Docetaxel, Cisplatin, and Fluorouracil was given to patients every 21 days with the following dosages per medication: Docetaxel: 60 mg/m$^2$, Day 1; Cisplatin: 60 mg/m$^2$, Day 1; 5-Fluorouracil: 600 mg/m$^2$ X 5 days. After perioperative chemotherapy patients considered resectable underwent subtotal/total gastrectomy. One hundred and thirty-four (88.7%) of the 151 patients receiving perioperative treatment were operated on. Complete resection was achieved in 123 (81.4%) of the 151 patients. The median disease-free survival (DFS) was 16 months (95% CI 22.5-31.5) and 5-year DFS was 25%. Median overall survival (OS) was 29 (95% CI, 21.9-36.0) months and 5-year OS was 29%. The presence of lymphovascular invasion and postoperative metastatic lymph node rate being ≥ 0.15 in the multivariate Cox regression analysis were determined as independent prognostic factors in terms of both DFS and OS. Our study has provided significant data in terms of sharing long-term real-life outcomes of perioperative mDCF. With mDCF combination in locally advanced gastric cancer, high R0 resection rates were obtained. Furthermore, our study put forward that MLR and LVI are two parameters that could be used in determining the prognosis of patients receiving perioperative mDCF.

**Keywords:** Locally advanced gastric cancer, Perioperative chemotherapy, Modified DCF, Prognostic factors

**Lokal İleri Mide Kanserinde Modifiye Dosetaksel, Sisplatin ve Fluorourasil Kombinasyonunun Etkinliği: Gerçek Yaşam Sonuçlarının Değerlendirilmesi**

Çalışmamızın amacı lokal ileri mide kanserli hastalarda perioperatif kemoterapi olarak modifiye dozda Dosetaksel, Cisplatin ve fFuorouracil (mDCF) kombinasyonun etkinliğinin ve gerçek yaşam sonuçlarının değerlendirilmesidir. Lokal ileri evre mide kanseri teşhisi ile perioperatif kemoterapi alan 151 hasta retrospektif incelendi. Perioperatif kemoterapi olarak mDCF; dosetaksel 60 mg/m$^2$; cisplatin 60 mg/m$^2$; 5-fluorouracil 600 mg/m$^2$ X 5 gün, 21 günde bir uygulandı. Perioperatif kemoterapi sonrası rezektabl olduğu düşünülen hastalara subtotal/total gastrektomi ve D2 lenf nodu diseksiyonu yapıldı. Perioperatif tedavi alan 151 hastanın 134'ü (%88.7) opere edildi. Yüz elli bir hastanın 123'ünde (%81.4) komplet (R0) rezeksiyon elde edildi. Median takip süresi 38 (14-118) ay idi. Median hastalıksız sağ kalım (DFS) 16 ay (%95 CI 22.5-31.5), median genel sağ kalım (OS) 29 ay (%95 CI 21.9-36.0) bulundu.

Yapılan multivariate Cox regresyon analizinde postoperatif metastatik lenf nodu oranının (MLR) ≥ 0.15 olması ve lenfovasküler invazyon (LVI) varlığı hem DFS hem de OS açısından bağımsız prognostik faktörler olarak belirlendi. Çalışmamız dosetaksel içeren perioperatif mDCF kombinasyonunun uzun dönem gerçek yaşam verilerinin paylaşılması açısından önemli bir veri niteliğindedir. Lokal ileri mide kanserinde mDCF kombinasyonu ile yüksek R0 rezeksiyon oranları elde edilmiştir. Ayrıca çalışmamızda perioperatif mDCF alan hastalarda MLR ve LVI'nin hastalığın prognozunu belirlemede kullanılabilecek parametreler olduğu gösterilmiştir.

**Anahtar Kelimeler:** Lokal ileri mide kanseri, Perioperative kemoterapi, Modifiye DCF, Prognostic faktörler

## INTRODUCTION

Gastric cancer is the fifth most common cancer in the world, ranking third in cancer-related deaths.[1,2] While 5-year survival is around 90% in patients with tumors not grown into the submucosa (T1)[3], this rate diminishes to 20% in patients with tumors grown into and through the submucosa or in patients with localized lymph node involvement.[4] Even though surgical treatments have favorable outcomes in early-stage diseases, post-operative recurrence/metastasis and related mortality constitute a major issue in locally advanced patients. Therefore, preoperative and/or postoperative numerous systemic treatments and/or radiotherapy modalities have been global research subjects.[5-12] Only 60-70% of radiologically operable patients can have their tumors completely resected (R0) in gastric cancer.[13] The most significant cause of mortality in operable patients is systemic tumor spread.[14] Thus, the perioperative chemotherapy approach has been suggested in this patient group to increase both R0 resection and survival rates by scheduling systemic treatment to an earlier time.[5,11] The superiority of perioperative chemotherapy to surgical treatment alone regarding overall survival has been shown for the first time in the study MAGIC (HR: 0.75; 95% Confidence interval (CI), 0.60 to 0.93; p= 0.009).[5] Similar results have been obtained in the FNCLCC/FFCD phase III trial comparing perioperative chemotherapy and surgery alone (HR: 0.69; 95% CI, 0.50 to 0.95; p= 0.02).[11] After having demonstrated the efficacy of Docetaxel addition to the standard regimen in metastatic gastric cancer in the V325 study[15], studies have started to focus on Docetaxel-containing combinations as perioperative chemotherapy regimens.[9,10,12] One of the first studies investigating the reliability and efficiency of Docetaxel in the perioperative chemotherapy regimen is the phase 2 NEOTAX study.[10] Following the phase 2 NEOTAX study, the phase 2 FLOT-4 study found pathologic complete response has been achieved at a higher rate particularly in intestinal-type gastric cancer with combinations of Docetaxel, Oxaliplatin, Fluorouracil and Leucovorin (FLOT) contrary to Epirubicin, Cisplatin, Fluorouracil/Epirubicin, Cisplatin, Capecitabine (ECF/ECX). However, survival outcomes of FLOT-4 have not been announced yet.[9]

Prognosis is more commonly associated with the surgical stage of patients with resectable gastric cancers. Local lymph node involvement, number of positive lymph nodes, and the depth of tumor invasion are associated with poor prognosis.[16,17] It has been indicated that the postoperative metastatic lymph node rate (MLR) in gastric cancer patients receiving neoadjuvant chemotherapy can be a prognostic factor.[18] The role of tumor grade, tumor size, and presence of lymphovascular invasion remains uncertain.[16,17] Our study aimed to show real-life data, disease-free survival (DFS), and overall survival (OS) results as well as the relation between clinicopathological features affecting these results in locally advanced gastric cancer patients receiving modified Docetaxel, Cisplatin and Fluorouracil (mDCF) regimen as perioperative chemotherapy.

## MATERIALS AND METHODS

Taken from the Medical Oncology Clinic of Ankara Numune Training and Research Hospital, 901 files of patients diagnosed with gastric cancer between the years 2014 and 2018 were reviewed. One hundred and fifty-one patients with locally advanced gastric cancer receiving perioperative chemotherapy as modified Docetaxel, Cisplatin and Fluorouracil (mDCF): Docetaxel 60 mg/m$^2$,

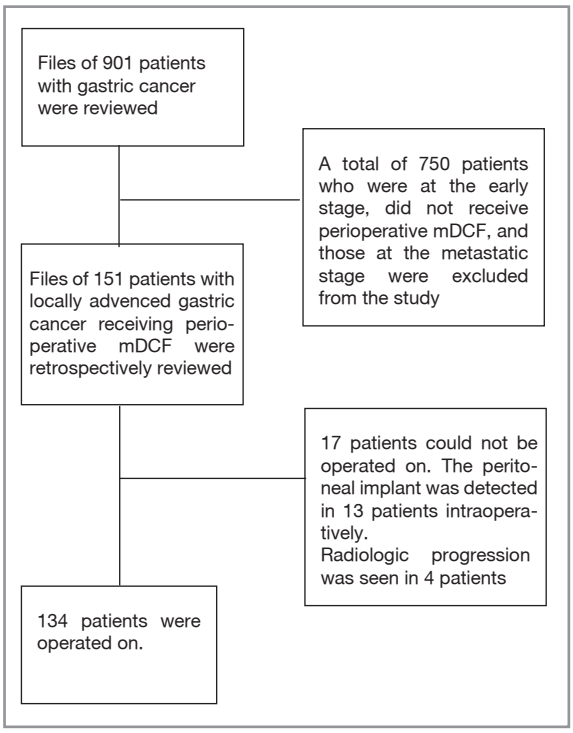


**Figure 1.** CONSORT diagram

Day 1; Cisplatin 60 mg/m², Day 1; 5-Fluorouracil 600 mg/m² X 5 days, every 21 days. Patients who were operated on due to early-stage gastric stage cancer, receiving perioperative chemotherapy besides mDCF, or those at a metastatic stage were excluded from the study (Figure 1). Patients with the Eastern Cooperative Oncology Group (ECOG) performance status between 0 and 2 were included in the study. Clinicopathological features, laboratory results, operative data, pathology reports, and treatment responses of the patients were analyzed. The patients were administered, according to their choice of physician, a 3-cycle mDCF, or chemoradiotherapy, and 1-cycle mDCF in the postoperative period.

The stage of each patient was determined through a thoracoabdominal computed tomography (CT). The clinical-stage of all patients was cT3-T4 or lymph-node-positive disease (cN+).

Patients receiving perioperative mDCF were evaluated with computed tomography 4-6 weeks after the last cycle. Patients considered resectable underwent subtotal/total gastrectomy and D2 lymph node dissection.

**Table 1.** Patient Demographics and Clinicopathological Features

| | n= 151 |
|---|---|
| Gender, male, n (%) | 118 (78.1) |
| Age, median year (min-max) | 59 (26-80) |
| ECOG | |
| 0, n (%) | 63 (41.7) |
| 1, n (%) | 77 (51.1) |
| 2, n (%) | 11 (7.2) |
| Tumor localization | |
| Antrum, n (%) | 37 (24.5) |
| Corpus, n (%) | 36 (23.8) |
| Esophagogastric junction, n (%) | 72 (47.7) |
| Total Gastric, n (%) | 5 (4.0) |
| Signet-ring cell histology, n (%) | 42 (27.8) |
| T stage at the time of diagnosis | |
| cT1-2, n (%) | 77 (50.9) |
| cT3-4, n (%) | 74 (49.1) |
| Lymph node at the time of diagnosis | |
| Positive, n (%) | 124 (82.1) |
| Negative, n (%) | 27 (17.8) |
| Grade | |
| 1, n (%) | 4 (2.6) |
| 2, n (%) | 10 (6.6) |
| 3, n (%) | 33 (21.9) |
| Unknown, n (%) | 104 (68.9) |

*ECOG= Eastern Cooperative Oncology Group*

The standard response evaluation criteria in solid tumors (RECIST 1.1) approach was used in the radiological evaluation of the treatment response.[19] A complete response was defined as the total disappearance of the clinically detected tumor in the preceding 4 weeks. Objective response rate (ORR) was defined as the total number of patients with complete and partial responses. Postoperative metastatic lymph node rate (MLR) was found by dividing the number of metastatic lymph nodes by the number of lymph nodes resected.

### Statistical Analysis

IBM Statistical Package for the Social Sciences 20 (SPSS) was used for statistical analyses. Statistical significance was set at $p< 0.05$. Chi-square or

**Table 2.** Response status according to RECIST criteria, postoperative staging/grading, and treatment

| | |
|---|---|
| Radiologic response (n= 151) | |
| Complete, n (%) | 1 (0.7) |
| Partial n (%) | 67 (44.4) |
| Stable, n (%) | 74 (49.0) |
| Progression, n (%) | 4 (2.6) |
| Unknown, n (%) | 5 (3.3) |
| Surgery(n:151) | |
| Subtotal, n (%) | 28 (18.5) |
| Total, n (%) | 106 (70.2) |
| None, n (%) | 17 (11.3) |
| Resection (n:151) | |
| R0, n (%) | 123 (81.4) |
| R1, n (%) | 10 (6.8) |
| R2, n (%) | 1 (0.8) |
| Not operated, n (%) | 17 (11.0) |
| Postop T stage (n:134) | |
| pT1-2, n (%) | 37 (27.6) |
| pT3-4, n (%) | 97 (72.4) |
| Postop N stage(n:134) | |
| Positive, n (%) | 90 (67.2) |
| Negative, n (%) | 44 (32.8) |
| Number of LN removed, mean (sd) (n= 134) | 25 (10-78) |
| Positive LN, mean (sd) (n= 134) | 4 (0-42) |
| LVI (N:134) | |
| Present, n (%) | 86 (64.2) |
| None, n (%) | 34 (25.4) |
| Unknown, n (%) | 14 (10.4) |
| Postoperative RT, n (%) (n= 134) | 112 (83.6) |
| Patients completing postoperative chemotherapy, n (%) (n= 134) | 88 (66) |

*LN= Lymph node*

Fisher's Exact test was used for the comparisons of independent categorical variables. Survival analysis was performed by the Kaplan-Meier estimator. Disease-free survival (DFS) was defined as the time elapsed from the time of diagnosis until disease recurrence or mortality. Overall survival (OS) was defined as the time elapsed from the time of diagnosis until mortality for any reason. Receiver operator characteristic (ROC) analysis was used to determine the optimum cut-off value of MLR in terms of DFS and OS. In determining the prognostic factors affecting DFS and OS, a multivariate COX regression model was formed with variables that had a p-value of < 0.20 as a result of the univariate analysis.

## RESULTS

### Demographics and Response to Therapy

Table 1 shows the demographic and clinicopathological features of 151 patients included in the study. The median age was 59 with a range of 26-80 years old. The majority of the patients were males (78.1%). The cT3-4 disease was present in 49.1% of the patients and lymph node positivity was found in 82.1% at the time of diagnosis. The number of preoperative chemotherapies had a median of 3 with a range of 2-4.

The objective response rate was found at 45.1% after perioperative chemotherapy, and radiologic progression was observed in 4 patients or 2.6% (Table 2). Curative surgery was performed in 89% of the patients. The complete resection rate (R0) was 81.4%. The pathological T3-T4 rate in the postoperative period was 72.4% and the pathological lymph node positivity rate was 67.2%. The chemotherapy completion rate in the postoperative period was 66%. Furthermore, 83.6% of patients received chemoradiotherapy postoperatively.

### Disease-Free Survival (DFS)

The median follow-up period was 38 months out of a total range of 14-118 months. The median DFS was 16 (95% CI, 22.5-31.5) months and 5-year DFS was 25%. In the univariate analysis, a cT3-4 stage at the time of diagnosis, a T stage of T3-4 postoperatively, postoperative lymph node positivity, postoperative metastatic lymph node rate (MLR) of ≥ 0.15, and presence of lymphovascular invasion (LVI) were found associated with decreased DFS (p= 0.010, p= 0.004, p= 0.001, p< 0.001, p= 0.003, respectively) (Table 3). In the multivariate COX regression analysis, MLR (HR 2.09, 95% CI, 1.10-3.97, p= 0.024) and LVI (HR 4.55, 95% CI, 1.37-15.14, p= 0.013) were found to be independent prognostic factors in terms of DFS (Table 4) (Figures 2A and 2B).

**Table 3.** Comparison of DFS and OS data of the patients according to clinicopathological features

| | n | DFS Median (95% CI) | 5-year DFS (%) | p | OS Median (95% CI) | 5-year OS (%) | p |
|---|---|---|---|---|---|---|---|
| Total | 151 | 16 (11-21) | 25 | - | 29 (22-36) | 29 | - |
| Gender | | | | | | | |
| Male | 118 | 15 (11-19) | 19 | 0.218 | 26 (17-35) | 25 | 0.251 |
| Female | 33 | 22 (15-29) | 34 | | 42 (23-60) | 42 | |
| Age | | | | | | | |
| <55 | 54 | 15 (13-17) | 21 | 0.664 | 26 (5-47) | 23 | 0.623 |
| ≥55 | 97 | 18 (11-25) | 30 | | 29 (24-34) | 37 | |
| ECOG at diagnosis | | | | | | | |
| 0 | 63 | 19 (10-28) | 28 | 0.543 | 30 (13-47) | 35 | 0.800 |
| 1-2 | 88 | 15 (8-22) | 27 | | 28 (23-33) | 30 | |
| Signet-ring cell histology | | | | | | | |
| Yes | 42 | 13 (11-15) | 17 | 0.055 | 17 (14-20) | 20 | 0.003 |
| No | 109 | 19 (11-27) | 27 | | 32 (23-40) | 32 | |
| T stage at diagnosis | | | | | | | |
| T1-2 | 77 | 27 (19-35) | 33 | 0.010 | 36 (8-63) | 42 | 0.034 |
| T3-4 | 74 | 13 (10-16) | 19 | | 29 (17-41) | 19 | |
| Lymph node at diagnosis | | | | | | | |
| Present | 124 | 16 (11-21) | 26 | 0.677 | 30 (22-38) | 48 | 0.829 |
| None | 27 | 26 (4-48) | 28 | | 37 (6-51) | 29 | |
| Grade at diagnosis | | | | | | | |
| 1-2 | 14 | 28 (0-59) | 40 | 0.248 | 38 (0-64) | 39 | 0.210 |
| 3 | 33 | 12 (8-16) | 28 | | 19 (6-32) | 21 | |
| Postoperative T stage | | | | | | | |
| T1-2 | 37 | 54 (29-71) | 43 | 0.004 | 56 (31-75) | 49 | 0.011 |
| T3-4 | 97 | 16 (13-19) | 23 | | 30 (20-40) | 27 | |
| Postoperative Lymph node | | | | | | | |
| Pozitive | 90 | 21 (14-28) | 20 | 0.001 | 30 (17-39) | 27 | 0.011 |
| Negative | 44 | 52 (18-68) | 54 | | 56 (20-71) | 49 | |
| Postoperative MLR | | | | | | | |
| < 0.15 | 67 | 44 (20-68) | 42 | < 0.001 | 56 (35-77) | 49 | 0.001 |
| ≥ 0.15 | 67 | 14 (12-16) | 19 | | 19 (9-29) | 24 | |
| Postoperative LVI | | | | | | | |
| Yes | 86 | 15 (13-17) | 20 | 0.003 | 28 (17-39) | 24 | 0.002 |
| No | 34 | 42 (20-51) | 47 | | 44 (21-53) | 49 | |

*ECOG= Easten Cooperative Oncology Group; MLR: Metastatic Lymph Node Ratio; LVI: Lymphovascular Invasion*

**Table 4.** Multivariate COX regression model of DFS and OS

| | DFS | | | OS | | |
|---|---|---|---|---|---|---|
| | HR | CI (95%) | p | HR | CI (95%) | p |
| Signet-ring cell histology | 1.180 | 0.645-2.160 | 0.592 | 1.933 | 0.992-3.776 | 0.053 |
| T stage at diagnosis (cT3-T4) | 0.994 | 0.560-1.764 | 0.983 | 1.272 | 0.664-2.438 | 0.469 |
| Postoperative T (pT3-T4) | 1.304 | 0.532-3.194 | 0.561 | 2.494 | 0.995-6.248 | 0.051 |
| Postoperative Lymph node (positive) | 1.439 | 0.462-4.486 | 0.530 | 0.874 | 0.231-3.306 | 0.842 |
| MLR (0,15 and higher | 2.094 | 1.104-3.972 | 0.024 | 2.783 | 1.240-6.244 | 0.013 |
| Postoperative LVI | 4.558 | 1.372-15.141 | 0.013 | 8.994 | 2.022-15.806 | 0.009 |

*MLR: Metastatic Lymph Node Ratio; LVI: Lymphovascular Invasion*

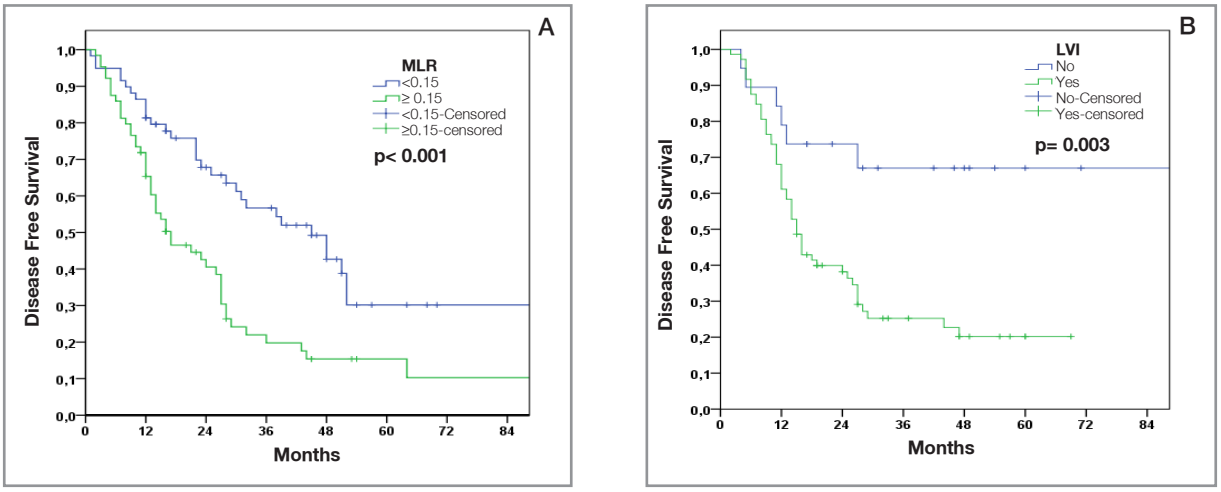


**Figure 2.** Kaplan-Meier survival curves **(A)** Association of DFS with MLR **(B)** Association of DFS with LVI

### Overall Survival (OS)

The median OS was 29 (95% CI, 21.9-36.0) months and 5-year OS was 29%. Univariate analysis, signet-ring cell histology, the cT3-4 stages at the time of diagnosis, the T3-4 stage postoperatively, the postoperative lymph node positivity, a MLR rate of ≥ 0.15, and presence of LVI were found associated with decreased OS ( p= 0.003, p= 0.034, p= 0.011, p= 0.011, p= 0.001, p= 0.002, respectively) (Table 3). Multivariate COX regression analysis revealed MLR (HR 2.78, 95% CI, 1.24-6.24, p= 0.013) and LVI (HR 8.99, 95% CI, 2.02-15.80, p= 0.009) to be independent prognostic factors in terms of OS (Table 4) (Figures 3A and 3B).

## DISCUSSION

The complete resection rate after perioperative mDCF in locally advanced gastric cancer was found to be 81.4% in our study. Furthermore, it was shown that MLR and LVI are prognostic factors in terms of DFS and OS.

While the R0 resection rate treated with surgery alone in locally advanced disease was between 40-60%, this rate increased to 60-90% with Docetaxel-based neoadjuvant/perioperative chemotherapy.[9,13,20-22] FLOT-4 study has reported a 74% R0 resection rate for the ECF/ECX group and an 85% resection rate for the FLOT group.[9] R0 resection rates were respectively as 69%, 87% and 64% in MAGIC, FNCLCC/FFCD and NEOTAX studies.[5,10,11] The reason for obtaining a lower R0 resection rate in the NEOTAX study when compared to the others can be associated with the fact that unresectable patients were also included in the NEOTAX study. Having achieved a better R0 resection rate in our and FLOT-4 studies compared to the MAGIC study, we consider that Docetaxel is a more efficient agent compared to Epirubicin.

It is known that neoadjuvant/perioperative chemotherapy has a downstaging effect on the T stage of the tumor and provides a positive contribution to survival.[5,9] The postoperative T3-4 rate in the chemotherapy group has been found as 48.3% and as 63.2% in the surgical group of the MAGIC study.[5] The preoperative T3-4 rate has decreased to 73% from 82% postoperatively in the ECF/ECX group and to 56% from 81% in the FLOT group in the FLOT-4 study.[9] In our study, while the preoperative T3-4 rate was 49.1%, it was found 72.4% in the postoperative period. Only computed tomography was used for the staging of the patients in our study, and endoscopic ultrasonography (EUS) and laparoscopy were not performed. The computed tomography was not evaluated by a single radiologist. Due to this, we consider that the preoperative T3-4 stage was calculated at a lower rate than the real radiologic T3-4 stage.

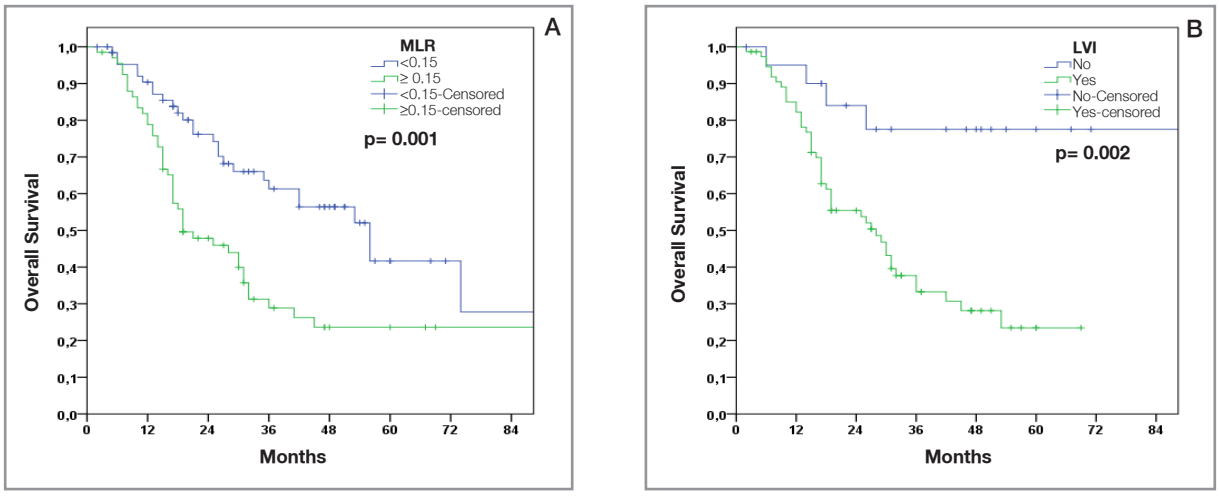


**Figure 3.** Kaplan-Meier survival curves **(A)** Association of OS with MLR **(B)** Association of OS with LVI

Perioperative chemotherapy explicitly decreases the postoperative lymph node positivity rate.[5,9] The postoperative lymph node positivity rate has been found at 68.9% in the chemotherapy group and 73.1% in the surgical group in the MAGIC study.[5] The lymph node positivity rate has decreased to 47% from 80% in the ECF group and to 41% from 77% in the FLOT group of the FLOT-4 study.[9] Similarly, in our study, lymph node positivity rate decreased to 67.2% from 82.1%.

The perioperative chemotherapy treatment has been beneficial in terms of both overall survival and disease-free survival through surgical resection alone has been carried out.[5,11] The FNCLCC/FFCD study has reported 5-year DFS as 34%[11] and NEOTAX study has presented median DFS as 11.9 months.[10] In our study, the 5-year DFS was found at 25% and the median DFS was found as 16 months. Patients with a lower esophagus (11%) and gastroesophageal junction (64%) tumors are the majority in FNCLCC/FFCD study.[11] In our study, 5-year DFS was found lower than the FNCLCC/FFCD study, since our study lacked patients with lower esophagus tumors, and the rate of patients with gastroesophageal junction tumors was low at 47.7%. The reason for the superiority of the median DFS in our study compared to the NEOTAX study was considered to be related to the fact that unresectable patients were included in the NEOTAX study.

The MAGIC study has found 5-year OS in patients receiving perioperative chemotherapy as 36%, and the same rate has been reported as 38% by the FNCLCC/FFCD study.[5,11] The median OS has been reported as 19 months in the NEOTAX study.[10] The 5-year OS and the median OS were determined as 29% and 29 months respectively in our study. The fact that OS is higher in our study compared to that of the NEOTAX study might be associated with the high postoperative positive lymph nodes (75.6%) and the inclusion of unresectable patients in the NEOTAX study. Having obtained a lower OS in our study than those of MAGIC and FNCLCC/FFCD, we considered this to have resulted from different rates of treatment after progression, the difference in the treatments received, and in the length of those treatments in both studies. The effect of adding Docetaxel to preoperative treatment on long-term survival is expected to become apparent with the announcement of the survival results of the FLOT-4 study.

Localized lymph node metastasis in non-metastatic gastric cancer is one of the most important prognostic factors. Similarly, some studies support that MLR is an important prognostic factor.[23-27] Ema et al. demonstrated that the MLR is an independent prognostic factor in patients with locally advanced gastric cancer receiving adjuvant chemotherapy and that while 5-year survival was 37% in those with an MLR of ≥ %16.7, it was found as 87% in

those with an MLR of <%16.7 (p< 0.001)[24]. In our study, MLR was detected as an independent prognostic factor in both DFS and OS, and 5-year overall survival for MLR< 15% and ≥ 15% groups were established as 49% and 24%, respectively.

Studies indicate the prognostic importance of lymphovascular invasion (LVI) in locally advanced gastric cancer.[28-30] In a retrospective study, LVI has been reported as an independent prognostic factor in patients with gastric cancer. The 5-year survival of patients with lymphovascular invasion and without LVI has been reported as 13% and 87%, respectively.[28] Similarly, in our study, LVI was found as an independent prognostic factor in terms of both DFS and OS. While the 5-year OS and DFS of patients with LVI were found as 24% and 20% respectively, in patients without LVI, rates were found as 49% and 47%.

Limitations of the study include the singular use of computed tomography for the staging of the patients, an EUS or laparoscopy was not performed for staging, and the computed tomographies were evaluated by different radiologists. Moreover, a lack of information on the dosage-density of the chemotherapy applied and on treatment-related toxicity are other limitations.

## Conclusion

Current phase 2 and phase 3 studies have indicated that the addition of Docetaxel to perioperative platinum and Fluorouracil combination regimens increases R0 resection and the pathological complete response rate. However, survival rates of one of these studies, namely FLOT-4, have not been announced yet. Our study provides significant data for understanding long-term real-life outcomes of perioperative chemotherapy containing Docetaxel, a current standard in treatment.

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