Original Article

Platelet-to-Lymphocyte Ratio and Neutrophil-to-Lymphocyte Ratio in Patients with Locally Advanced Gastric Cancers

Lokal İleri Mide Kanserli Hastalarda Trombosit Lenfosit Oranı ve Nötrofil Lenfosit Oranı

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ABSTRACT

Aim: This study aimed to determine the relationship between preoperative neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) levels with prognosis of locally advanced gastric cancers (GC).

Methods: This was a retrospective single centre study conducted between January 2011 and January 2016 at the Department of General Surgery of Osmangazi University Medical Faculty. A total of 83 patients histologically diagnosed with GC who received curative surgery were included in the study.

Results: Median (first-third quartile) NLR value was 2.62 (1.93-4) and PLR value was 148.1 (117.73-221.43). ROC analysis did not yield optimal cut-off values for NLR and PLR to predict mortality. Lower overall survival rates were reported in GC patients with extracapsular invasion, perineural invasion, lymphovascular invasion, surgical margin positivity, various clinical findings (leakage, infection and recurrence), and lower albumin level (all, $p<0.05$). Cox regression analysis demonstrated that preoperative NLR and PLR were non-significant factors for mortality ($p=0.302$ and 0.147, respectively). Tumour size, perineural invasion, N3 stage, leakage and lower albumin level were independent prognostic determinants for mortality.

Conclusion: Our results indicate that preoperative NLR and PLR were not associated with prognosis and could not be used as prognostic indicators for mortality in patients with GC. Greater tumour size, perineural invasion, N3 stage, leakage and hypoalbuminemia were significantly associated with prognosis. Further prospective studies with longer patient follow-up and larger sample sizes will help to verify our current data on prognostic indicators for GC.

Keywords: Gastric cancer, NLR, PLR, prognosis, overall survival

ÖZET

Amaç: Bu çalışma, ameliyat öncesi nötrofil-lenfosit oranı (NLO) ve trombosit-lenfosit oranı (PLO) düzeylerinin mide kanserinin (MK) prognozu ile ilişkisini belirlemeyi amaçladı.

Gereç ve Yöntem: Bu, Ocak 2011-Ocak 2016 tarihleri arasında Eskişehir Osmangazi Üniversitesi Tıp Fakültesi Genel Cerrahi Kliniğinde yürütülen retrospektif tek merkezli bir çalışmadır. Çalışmaya histolojik olarak GK tanısı konan ve küratif cerrahi uygulanan toplam 83 hasta dahil edildi.

Bulgular: Medyan (1.-3. çeyrek) NLO değeri 2.62 (1.93-4) ve PLO değeri 148.1 (117.73-221.43) idi. NLO ve PLO ile mortaliteyi tahmin etmek için yapılan ROC analizinde uygun bir kesim noktası elde edilmedi. Ekstrakapsüler invazyon, perinöral invazyon, lenfovasküler invazyon, cerrahi sınır pozitifliği, çeşitli klinik bulgular (sızıntı, enfeksiyon ve nüks) ve düşük albümin düzeyi ($p<0.05$) olan MK hastalarında daha düşük genel sağkalım oranları belirlendi. Cox regresyon analizi, preoperatif NLO ve PLO'nun mortalite için anlamlı olmayan faktörler olduğunu gösterdi (sırasıyla $p=0,302$ ve 0,147).

First Received: 23.12.2021, Accepted: 22.02.2022 doi: 10.5505/aot.2022.36450

Tümör boyutu, perinöral invazyon, N3 evresi, sızıntı ve düşük albümin düzeyi mortalite için bağımsız prognostik belirleyiciler olarak bulundu.
Sonuç: Sonuçlarımız, preoperatif NLO ve PLO'nun prognozla ilişkisinin olmadığını ve MK'li hastalarda mortalite için prognostik göstergeler olarak kullanılamayacağını göstermektedir. Daha büyük tümör boyutu, perinöral invazyon, N3 evresi, sızıntı ve hipoalbüminemi prognoz ile anlamlı olarak ilişkiliydi. Hastaların daha uzun süre takip edildiği ve daha büyük örneklem büyüklüklüğüne sahip ileri prospektif çalışmalar, MK için prognostik göstergeler hakkındaki mevcut verilerimizi doğrulamaya yardımcı olacaktır.

Anahtar Kelimeler: Mide kanseri, NLO, PLO, prognoz, genel sağkalım

Introduction

Gastric Cancer (GC) is the third leading cause of cancer-associated mortality, causing about 800,000 deaths worldwide, partially because most patients are diagnosed at an inoperable, advanced stage of disease [1]. Patients usually present with regional or distant metastasis at the time of diagnosis, and their overall 5-year survival still remains below 50%, even with potentially curative surgery [2]. Management approaches to GC are primarily based on clinical prognosis assessment via the tumour node metastasis (TNM) staging system, but patients defined to have the same TNM stage demonstrate heterogeneous clinical course and varying prognosis [3]. In addition, some methods, including magnetic resonance imaging, computed tomography and endoscopic ultrasonography, may be helpful in predicting preoperative tumour stage and prognosis to some extent, but they are expensive and do little to eliminate uncertainty [4]. The ability to identify individualized risk factors and estimate prognosis are essential to implement optimal management and follow-up strategies. Although various factors have been investigated to classify survival in patients with GC, there is still an urgent need for timesaving, reliable and routine prognostic indicators associated with prognosis.

Recently, in vivo and in vitro studies have reported that the tumour microenvironment is associated with both systemic and local inflammatory response and may play a critical role in cancer tumorigenesis and progression through tumour proliferation, invasion, angiogenesis and metastasis [5]. Given the relationship between inflammatory response and overall survival, inflammation-based parameters, including C-reactive protein, IL-6, albumin, Glasgow prognostic score, platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR), have been demonstrated to have prognostic value in cancer patients [6]. NLR and PLR are determined simply, by routine laboratory assessment and are widely used to assess the extent of systemic inflammatory response for various types of cancer and have been valuable to predict prognosis in patients with cancer [7]. However, the prognostic significance of preoperative NLR and PLR levels for GC remains complicated and imprecise.

The aim of the study was to determine the associations between preoperative NLR and PLR values and clinicopathological features of locally advanced GC and to investigate their prognostic value in locally advanced GC patients who underwent surgery.

Materials and Methods

This was a retrospective single centre study conducted between January 2011 and January 2016 at the Department of General Surgery of Osmangazi University Medical Faculty. Ethical approval was obtained from the local ethics committee. A total of 83 patients histologically diagnosed with GC who received curative surgery were included in the study. The inclusion criteria for patients involved the following criteria: histo-pathologically proven diagnosis of GC,

complete clinical and follow-up data, and presence of all relevant preoperative biochemical data, including complete blood count (CBC) and albumin levels. Patients with anaemia, hepatic disorder, acute infection, autoimmune or endocrine disorders, haematological diseases, remnant gastric cancer, synchronous or metachronous cancer, those using corticosteroids in the last six months or any medication that could affect biochemical analyses, and those had received neoadjuvant therapy or had undergone emergency gastrectomy for bleeding or perforation were excluded from the study. In total, 20 patients were excluded due to these exclusion criteria. All research procedures were assessed and approved by the Research Ethics Committee of Osmangazi University and were carried out in agreement with the ethical standards specified in the Declaration of Helsinki. Written informed consent from patients was deemed unnecessary due to the retrospective design of our study.

Demographic characteristics, clinical data (histology, size, differentiation and primary location of GC), type of surgical intervention, Lauren classification, clinical TNM stage (in accordance with the pathological classification criteria of American Joint Committee on Cancer Staging/UICC-TNM for GC), the numbers of lymph nodes and metastatic lymph nodes, presence of perineural, lymphovascular or extracapsular invasion, the length of hospitalization, and clinical outcomes, including the presence of leakage or infection, recurrence status and final status were obtained from the hospital records of each patient [8,9]. Patients were evaluated with clinical and radiological examinations every 3 to 6 months. Clinical outcomes, including recurrence and causes of death were examined through reviewing medical records or direct questioning of a family member. The last follow-up examination was carried out in January 2016. Overall survival (OS) was defined as the time from the date of performed surgical procedures to the date of last follow-up or mortality.

Blood samples were obtained preoperatively from the antecubital vein for the measurement of CBC and albumin. Complete blood count, including neutrophil and lymphocyte levels, platelet count and haemoglobin value, was measured with the Mindray BC-6800 auto-analyser (Mindray Electronics Co, Ltd, Shenzhen, China). The NLR was calculated as the neutrophil level divided by the lymphocyte level. The PLR was determined as the platelet count divided by the lymphocyte level. Serum albumin levels were determined via the photometric method on an ADVIA 2400 autoanalyzer (Siemens, Munich, Germany). Analytical procedures of all biochemical markers were carried out within one hour after venepuncture.

Statistical analysis

All analyses were performed on SPSS v21 (IBM, Armonk, NY, USA). For the normality check, the Kolmogorov-Smirnov test with Lilliefors correction was used. Data are given as mean ± standard deviation or median (first quartile-third quartile) for continuous variables according to normality of distribution, while frequency (percentage) was used for categorical variables. NLR and PLR of the alive and mortal cases were analysed with the Mann-Whitney U test. Survival times were calculated with the Kaplan-Meier method. Between-group comparisons of the survival times were performed with the Log rank test. We included age and gender as main characteristics, continuous variables and the factors which were found to be significant ($p<0.05$) in Kaplan Meier Analysis as univariate analysis into multivariate analysis and further checked these factors with Cox regression analysis (forward conditional method). p values of <0.05 were accepted as statistically significant results.

Results

The mean age of patients with GC was 63.82 ± 13.97 years and most of them were male (n = 56, 67.47%). Gastric adenocarcinoma was diagnosed in 56 (67.47%) patients, singlet ring cell adenocarcinoma in 25 (30.12%) patients, and mucinous adenocarcinoma in two patients according to histopathological examinations. Surgical procedures were: total gastrectomy in 59 (71.08%) patients, subtotal gastrectomy in 23 (27.71%) patients, and laparoscopic total gastrectomy in one patient. Tumour locations were: the distal third in 30 (36.14%) patients, the central third in 25 (30.12%) patients, and the proximal third in 24 (28.92%) patients. Linitis plastica was present in four (4.82%) patients. Thirty-four (40.96%) patients presented with extra-capsular invasion, 59 (71.08%) with perineural invasion and 53 (63.86%) with lymphovascular invasion. Adjuvant chemo-therapy was applied to 72 (86.75%) patients, while adjuvant radiotherapy was applied to 52 (62.65%) patients. During the follow-up period, recurrence was found in 33 (39.76%) patients and 64 (77.11%) patients died.

The median lymphocyte count was 1.6 (1.3-2.1) 103/µL, and neutrophil count was 4.8 (3.7-5.5) 103/µL. Mean platelet count was found to be 268.93 ± 90.69 103/µL. Haemo-globin values were 11.89 ± 1.98 g/dL. Laboratory results and clinical characteristics of GC patients are shown in Table 1. Median NLR was 2.60 (IQR: 1.89 - 4.00) in alive cases and was 2.65 (IQR: 1.93 - 4.04) in mortal cases (p=0.573). Median PLR was 138.00 (IQR: 116.80- 183.33) in alive cases and was 150.82 (IQR: 121.36- 221.79) in mortal cases (p=0.380). We performed ROC analysis to obtain optimal cut-off values for preoperative NLR and PLR values that could predict mortality in GC patients. However, analyses did not yield appropriate cut-off values for NLR and PLR to predict mortality (data not shown).

The Kaplan-Meier method was used to evaluate 5-year OS rates and comparison of variables was performed with Log rank test (Table 2). OS rates were 29.1 ± 5.2 % for all patients. Lower OS was reported in GC patients with extracapsular invasion, perineural invasion, lymphovascular invasion, surgical margin positivity and various clinical outcomes (leakage, infection and recurrence). Those with lower albumin levels also had lower OS rate (all, $p<0.05$). Patients with stage 3&4 tumours showed reduced OS rates than those with stage 1&2 ($p<0.001$). Patients presenting with T4 or N3 demonstrated lower OS rate compared to other stages ($p<0.001$). Age (<65) ($p = 0.450$), gender ($p = 0.482$), surgical procedure ($p = 0:165$), differentiation ($p = 0.241$), histology ($p = 0.442$), Lauren classification ($p = 0.064$), location ($p = 0.205$), lymph node dissection ($p = 0.139$), adjuvant chemotherapy ($p = 0.820$), and adjuvant radiotherapy ($p = 0.204$) were not associated with survival.

Cox regression analysis was performed to determine the best prognostic factors associated with mortality. Higher tumour size, the presence of perineural invasion, N3 stage, leakage, and lower albumin level were poor prognostic determinants for mortality (Table 3). Patients presenting with perineural invasion had a 2.481-fold higher risk of mortality than those without (HR: 2.481, 95% CI: 1.271-4.843, p=0.008) (Figure 1). Patients admitted with N3 stage tumour showed a 2.967-fold higher risk of death than other patients (HR: 2.967, 95% CI: 1.674-5.260, $p<0.001$) (Figure 2). Patients with leakage had an 8.546-fold higher risk of mortality than those without (HR: 8.546, 95% CI: 4.108-17.780, $p<0.001$) (Figure 3). Preoperative NLR and PLR were shown to be non-significant factors for mortality (p=0.302 and 0.147, respectively). Other variables included in the model, age (p=0.138), gender (p=0.106),

Table 1. Laboratory results and clinical characteristics of gastric cancer patients

Time between diagnosis and operation, days	16 (9 - 23)
Differentiation	
Poor	49 (59.04%)
Moderate	21 (25.30%)
Well	13 (15.66%)
Lauren classification	
Intestinal	35 (42.17%)
Diffuse	37 (44.58%)
Mixed	11 (13.25%)
Tumor size, mm	50 (30 - 80)
Number of lymph nodes	19 (13 - 33)
Number of metastatic lymph nodes	4 (1 - 13)
Lymph node dissection	
D1	18 (21.69%)
D2	41 (49.40%)
D1+	2 (2.41%)
D2+	22 (26.51%)
Surgical margin positivity	9 (10.84%)
T stage	
T1	12 (14.46%)
T2	4 (4.82%)
T3	34 (40.96%)
T4	33 (39.76%)
N stage	
N0	20 (24.10%)
N1	15 (18.07%)
N2	21 (25.30%)
N3	27 (32.53%)
M stage	
M0	82 (98.80%)
M1	1 (1.20%)
Length of stay in hospital, days	9 (6 - 12)
Leakage	13 (15.66%)
Infection	21 (25.30%)
Albumin, g/dL	3.96 ± 0.57
Neutrophil / Lymphocyte ratio	2.62 (1.93 - 4.00)
Platelet / Lymphocyte ratio	148.10 (117.73 - 221.43)
Follow-up time, months	25 (7 - 53)

Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

Table 2. Survival times (months) with Kaplan Meier method and comparisons of groups with Log rank test

	n	Exitus	Median (95.0% CI)	5-years survival rate (%)	p
Overall survival	83	64	25 (17.74 - 32.26)	29.1 ± 5.2	N/A
Extracapsular invasion					
Absent	49	32	51 (20.89 - 81.11)	45.9 ± 7.5	<0.001
Present	34	32	13 (8.72 - 17.28)	5.9 ± 4.0	
Perineural invasion					
Absent	24	13	67 (36.98 - 97.02)	59.1 ± 10.6	<0.001
Present	59	51	14 (8.36 - 19.65)	17.5 ± 5.1	
Lymphovascular invasion					
Absent	30	16	81 (39.32 - 122.68)	56.6 ± 9.6	<0.001
Present	53	48	14 (10.95 - 17.05)	14.3 ± 4.9	
Surgical margin					
Negative	74	55	28 (18.97 - 37.03)	32.7 ± 5.7	<0.001
Positive	9	9	7 (0.00 - 15.77)	0.0 ± 0.0	
T stage					
T1 & T2	16	9	75 (37.01 - 112.99)	59.3 ± 12.9	0.002
T3	34	26	27 (19.97 - 34.03)	33.6 ± 8.4	
T4	33	29	13 (7.37 - 18.63)	10.6 ± 5.6	
N stage					
N0	20	9	84 (69.26 - 98.74)	78.6 ± 9.5	<0.001
N1	15	10	41 (11.67 - 70.33)	36.0 ± 13.3	
N2	21	18	15 (3.04 - 26.96)	11.4 ± 7.4	
N3	27	27	13 (8.00 - 18.00)	3.7 ± 3.6	
TNM stage					
Stage 1	12	5	84 (62.79 - 105.21)	81.8 ± 11.6	<0.001
Stage 2	14	9	61 (20.39 - 101.61)	53.9 ± 14.1	
Stage 3 & 4	57	50	14 (10.83 - 17.17)	12.4 ± 4.6	
Leakage					
Absent	70	51	28 (14.09 - 41.91)	34.7 ± 5.9	<0.001
Present	13	13	2 (0.00 - 4.35)	0.0 ± 0.0	
Infection					
Absent	62	44	34 (17.41 - 50.59)	35.9 ± 6.4	0.001
Present	21	20	11 (2.03 - 19.97)	9.5 ± 6.4	
Recurrence					
Absent	50	32	45 (0.00 - 101.85)	48.6 ± 7.2	0.010
Present	33	32	23 (17.37 - 28.63)	3.0 ± 3.0	
Albumin					
< 3.5	15	14	4 (0.00 - 9.05)	20.0 ± 10.3	0.007
≥ 3.5	68	50	27 (17.10 - 36.90)	30.9 ± 5.9	

CI: Confidence interval. Same letters denote the lack of statistically significant difference between groups.

Table 3. Significant prognostic factors of the mortality, Cox regression analysis

	β Coefficient	Std Error	p	Exp(β)	95.0% CI for Exp(β)	
Tumor size	0.009	0.003	0.008*	1.009	1.002	1.016
Perineural invasion	0.909	0.341	0.008*	2.481	1.271	4.843
N3 stage	1.088	0.292	<0.001*	2.967	1.674	5.260
Leakage	2.145	0.374	<0.001*	8.546	4.108	17.780
Albumin	-0.556	0.234	0.017*	0.574	0.363	0.907

CI: Confidence interval.
*p value <0.05 significant

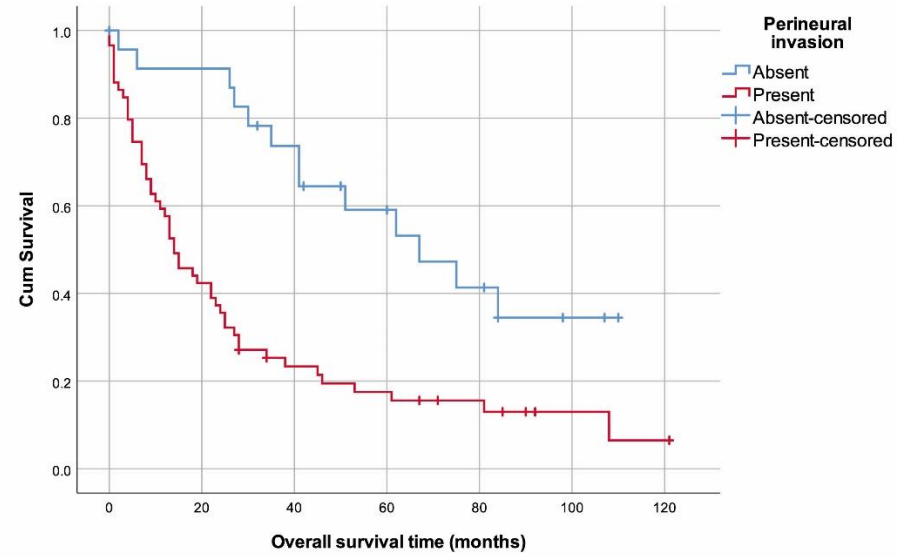

Figure 1. Overall survival plot with regard to perineural invasion

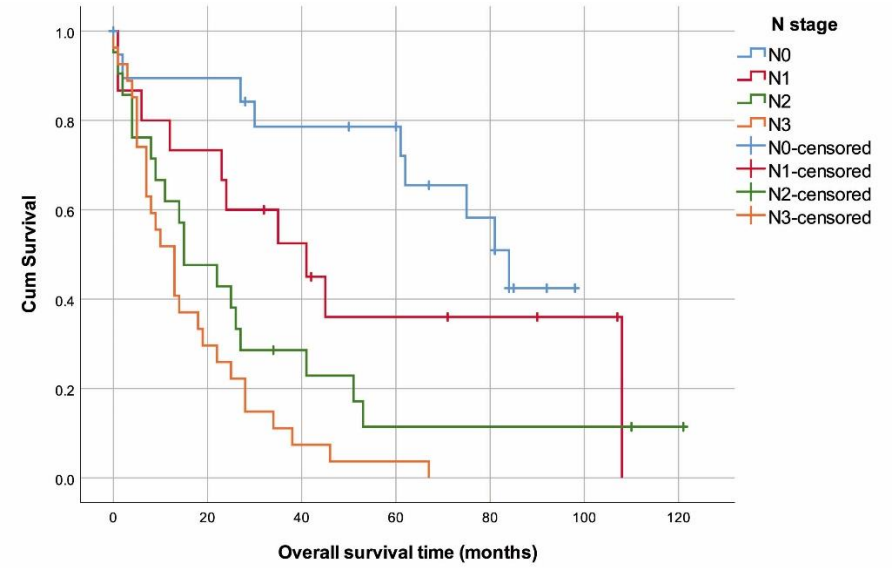

Figure 2. Overall survival plot with regard to N stage

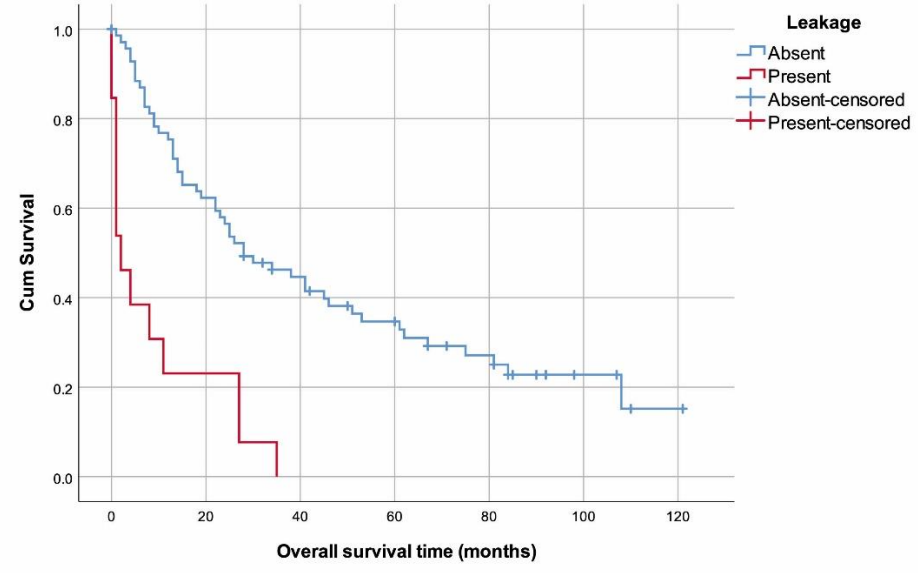

Figure 3. Overall survival plot with regard to leakage

time between diagnosis and surgery (p=0.263), total number of lymph nodes (p=0.659), number of metastatic lymph nodes (p=0.463), extracapsular invasion (p=0.305), lymphovascular invasion (p=0.264), surgical margin positivity (p=0.246), T stage (p=0.130), TNM stage (p=0.448), infection (p=0.456), recurrence (p=0.273), and haemoglobin (p=0.651) were also found to be non-significant.

Discussion

This study aimed to determine possible relationships between preoperative NLR and PLR levels and the clinical characteristics of locally advanced GC, and to assess whether they had predictive significance on disease prognosis. Contrary to previous literature, we did not obtain optimal cut-off values for PLR and NLR to predict mortality, and we demonstrated that preoperative NLR and PLR were non-significant determinants for prognosis in patients with locally advanced GC. We showed that greater tumour size, presence of perineural invasion, N3 stage, leakage, and also lower albumin levels may be poor prognostic predictors for mortality in patients with locally-advanced GC.

Cancer-related inflammation has been described as a substantial cross-talk factor associated with neoplastic growth since it was first suggested by Virchow in the 19th century [10]. In the tumour microenvironment, stromal cells around tumours recruit cytokine-producing inflammatory cells which could facilitate cancer progression in association with proliferation, resistance to apoptosis, induction of angiogenesis, evasion of growth suppressors, development of replicate immortality and activation of invasion and metastasis [2]. Neutrophils may have a critical role in cancer development and progression through pro-angiogenic factors, inflammatory mediators and matrix metalloproteinases [11]. Furthermore, increased neutrophil count in the tumour microenvironment can suppress the antitumor properties of activated T cells and the cytolytic function of immune cells, while also possibly limiting lymphoplasmacytic reactions in tumour cells [12]. Lymphocytes may exhibit a significant role as extrinsic tumour suppressors by attacking and eliminating tumour cells at the outset of tumorigenesis [13]. Patients who have decreased lymphocyte count may have suppressed cell-mediated immune response

against cancer. In addition, platelets may contribute to the inflammatory response by augmenting angiogenesis or releasing growth factors [3]. Thus, cancer-related inflammation may be related with thrombocytosis, leucocytosis, neutrophilia and lympho-cytopenia.

An increase in PLR or NLR may reflect the cancer-related inflammatory status, and these parameters have been broadly examined as potential prognostic factors in many types of solid tumours. Szor et al., in a systematic review and meta-analysis of seven studies comprising 3264 resected GC patients, demonstrated that elevated NLR was associated with lower 5-year OS, older age, male sex, elevated tumour invasion depth, and nodal involvement [14]. Sun et al. showed in a systematic review and meta-analysis of 19 studies comprising 5431 GC patients that increased preoperative NLR was associated with poor OS and progression-free survival [13]. Again, Cao et al. reported in a meta-analysis of 28 studies comprising 15617 patients that increased PLR was related with poor OS in GC, but noted significant publication bias [15]. In contrast, Wang et al. demonstrated in 324 GC patients who had undergone resection for stage 3 cancer that preoperative NLR and PLR were not prognostic and were not associated with disease-free survival and OS [16]. Zamiri et al. reported no significant relationship between NLR and the duration of disease-free survival in 164 patients with non-metastatic and operable GC [17]. Xu et al. revealed in a meta-analysis of 8 studies involving 4513 patients that PLR may not be used as a prognostic indicator for OS in patients with GC [4].

Our study is among the latter group; we did not find optimal NLR or PLR cut-off values that could estimate mortality in patients with locally advanced GC who had undergone resection. We also showed that NLR and PLR had no prognostic association with OS in locally advanced GC patients. This may be related to patients' characteristics; however, the overall controversy in this topic appears to suggest the presence of various biases and confounding factors. For instance, previous studies have demonstrated that sex, race, ethnic heterogeneity and tumour type could influence prognosis and prognostic indicators in GC [18]. Due to the retrospective nature of our study, these factors are also likely to have caused bias in our results. Several conditions, including treatment and concurrent hidden infection(s), could influence the levels of NLR and PLR. Although our study attempted to exclude patients with certain conditions, including acute infection or inflammatory diseases, the retrospective design of this study may not have been able to completely exclude patients with external sources of inflam-matory reactions that were undetectable when blood samples were drawn. In addition, shorter follow-up may have impacted obtained results. Another possible explanation is the relatively small number of GC patients included and unconfirmed cut-off values for preoperative PLR and NLR. Previous studies have shown diverse cut-off values for PLR and NLR in predicting survival [19]. The lack of consensus on cut-off values for PLR and NLR remains a critical issue and shows the need to exercise caution when considering the clinical use of these parameters.

The basis for inconsistent results throughout the literature remains poorly understood and should be another cause of concern. Not with standing the possible sources of error in measurements from centre to centre, the likely presence of publication bias and all's well literature bias could have contributed to a sustained publication of studies reporting value for PLR and NLR in determining prognosis or other disease-related characteristics. This is not unusual, as reports of so-called 'biomarkers' in the literature are almost always positive. For example, an analysis of more than 1900 publications

demonstrated that about 95% of 'cancer biomarker/indicator' studies showed positive results [20]. Publication bias is a well-established phenomenon in medical research, and is caused by refraining from submission of non-significant results or by the generally negative decisions of editors towards such studies. Recording and analysing NLR and PLR data is a simple process that needs only accurate data which can be easily reached through hospital databases. Authors who found no significance in these short assessments are very likely to have decided to avoid publication due to the arduous process of writing their findings as a full article and their established understanding that these results would be unlikely to receive recognition by journals. Indeed, meta-analyses have shown that publication bias may influence the ever-growing body of literature concerning PLR and NLR assessment [21].

Many clinicopathological determinants, such as clinical stage, pathological TNM stage, depth of tumour invasion, tumour size and lymph node metastasis, may affect the prognosis in GC patients. While many researchers continue to investigate various prognostic factors, TNM staging, despite its limitations, is currently accepted to be a crucial prognostic tool. In addition, Yamashita et al. demonstrated that metastatic lymph node ratio was a good prognostic factor in GC patients [22]. Wang et al. revealed in 430 advanced GC patients that tumour invasion, lymph node metastasis, and tumour size were independent prognostic factors [23]. Crumley et al. demonstrated a relationship between low albumin levels and poor survival in patients with GC, dependent on increased levels of C-reactive protein [24]. Hypo-albuminemia may reflect poor nutritional status and increased inflammatory degree, potentially adversely affecting the survival of GC patients. Consistent with the literature, we found that higher tumour size, the presence of perineural invasion, N3 stage, leakage and lower albumin levels were independently associated with mortality and disease prognosis. These factors may be used as prognostic indicators and could be valuable to identify patients at high risk of mortality. Further prospective studies with longer patient follow-up and larger sample sizes will help verify our current data on prognostic indicators for GC.

The study has several limitations. First, the study was conducted as a single-centre, retrospective cohort that included a relatively small sample size, which may have caused bias in results. Second, we were unable to determine those who died from non-GC causes during the follow-up period. This resulted in the failure to identify disease-specific survival rates.

Conclusion

In this study, our results indicate that preoperative NLR and PLR were non-significant factors for prognosis and could not be used as prognostic indicators for mortality in patients with locally advanced GC. Greater tumour size, perineural invasion, N3 stage, presence of leakage, and hypoalbuminemia were independently associated with post-operative mortality and disease prognosis. Future studies could aim to include a greater number of patients with early-stage disease in order to be able to compare parameters with better prognostic resolution and to increase the follow-up time of patients.

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Doi: 10.5505/aot.2022.36450

