

Received: 2021.06.04

Accepted: 2021.10.11

Available online: 2021.10.27

Published: 2022.01.31

# Utility of Pretreatment Blood Platelet-To-Lymphocyte Ratio in Prediction of Clinical Outcomes and Chemosensitivity in Patients with Advanced Gastric Cancer: A Meta-Analysis

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
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**Financial support:** This study was supported by Hubei Municipal Health and Family Planning Commission (No. WJ2017Q034), and Wuhan Municipal Health and Family Planning Commission (No. WX16E11)

**Conflict of interest:** None declared

**Background:** The results of previous studies that evaluated the association between pretreatment blood platelet-to-lymphocyte ratio (PLR) and clinical outcomes and chemosensitivity in patients with advanced gastric cancer are inconsistent. Therefore, this study was designed to investigate the association between pretreatment blood PLR and clinical outcomes and chemosensitivity in advanced gastric cancer patients.

**Material/Methods:** We performed a systematic literature search in PubMed, Web of Science, EMBASE, and the Cochrane Library up to Mar 9, 2021. Hazard ratios (HRs) for overall survival (OS) and disease-free survival (DFS) were pooled for meta-analysis. The quality of the included studies was measured by the Newcastle-Ottawa Quality Assessment Scale.

**Results:** We included 17 studies comprising 3499 patients with advanced GC in this meta-analysis. Pooled results demonstrated that high PLR was correlated with poor OS (HR=1.429, 95% CI=1.246-1.639,  $P<0.001$ ) and DFS (HR=1.47, 95% CI=1.14-1.88,  $P=0.003$ ) compared with low PLR in patients with advanced GC. Moreover, high PLR was associated with a lower response to chemotherapy in patients with advanced GC (OR=1.395, 95% CI=1.056-1.841,  $P=0.019$ ). However, there was no significant correlation between PLR and clinicopathological features.

**Conclusions:** This meta-analysis suggests that high PLR is a risk factor for unfavorable OS, DFS, and chemosensitivity in patients with advanced GC.

**Keywords:** **Meta-Analysis • Prognosis • Stomach Neoplasms**

**Full-text PDF:** <https://www.medscimonit.com/abstract/index/idArt/933449>

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## Background

Gastric cancer (GC), a global problem of human health, is the fifth most common malignancy and the third leading cause of cancer-related death worldwide [1]. Annually, there are more than 1 033 701 newly diagnosed patients with GC [2]. Tumor stage is the strongest prognostic factor for patients with GC; it is a potential curative disease at an early stage, but it is almost always diagnosed at the advanced stage of disease [3]. Although great progress has been made in the diagnosis and treatment of gastric cancer, the outcome of advanced gastric cancer is still extremely poor [4]. The role of surgical treatment still remains quite significant in conquering GC [5]. For patients with advanced GC, adequate surgical resection is not the only curative therapeutic regimen [6], and chemotherapy is regarded as an important part of or main treatment in advanced GC patients [7]. However, the response rate to first-line treatment is only 27-54%, and many patients who show no response to chemotherapy have fatal outcomes because of delayed effective therapy [8,9]. There are still no consistent and recognized biomarkers for chemotherapeutic drugs in advanced GC patients; therefore, a predictive biomarker for prognosis and prediction of chemosensitivity to improve therapeutic strategies in patients with advanced GC is required.

Studies have demonstrated that the prognosis of different types of cancer is influenced not only by its features, but also by the tumor microenvironment derived from the immunological state of the patient [10-12]. Recently, studies have assumed that the systemic inflammatory response has a critical role in the occurrence and progression of cancer, as well as in the response to therapy [13-16]. Pretreatment systemic inflammation response biomarkers, such as hypersensitive C-reactive protein (hs-CRP), PLT count, platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and lymphocyte-to-monocyte ratio (LMR) have been identified as prognostic indicators in a variety of malignant tumors, including GC [17-20]. Liu et al showed that PLR is associated with response to chemotherapy and OS in patients with advanced non-small cell lung cancer [21]. Among these prognostic biomarkers, the prognostic value of PLR in GC may be the most controversial [22,23]. The utility of PLR for prediction of prognosis and chemosensitivity in patients with advanced GC is unclear. Thus, we conducted a meta-analysis to evaluate the utility of PLR in prediction of prognosis and chemosensitivity, as well as the correlations between the pretreatment PLR and clinicopathological features, in patients with advanced GC.

## Material and Methods

### Literature Search

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Review and

Meta-Analysis (PRISMA) guidelines [24] and it was conducted according to the mandatory 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and checklist. We conducted a comprehensive literature search in PubMed, Web of Science, EMBASE, and the Cochrane Library up to March 9, 2021. The search strategy was (“Neoplasm, Stomach” or “Stomach Neoplasm” or “Neoplasms, Stomach” or “Gastric Neoplasms” or “Gastric Neoplasm” or “Neoplasm, Gastric” or “Neoplasms, Gastric” or “Cancer of Stomach” or “Stomach Cancers” or “Gastric Cancer” or “Cancer, Gastric” or “Cancers, Gastric” or “Gastric Cancers” or “Stomach Cancer” or “Cancer, Stomach” or “Cancers, Stomach” or “Cancer of the Stomach” or “Gastric Cancer, Familial Diffuse”) AND (“PLR” or “platelet/lymphocyte ratio” or “platelet to lymphocyte ratio” or “platelet lymphocyte ratio” or “platelet-to-lymphocyte ratio” or “platelet-lymphocyte ratio”). The references were manually examined to collect potentially relevant studies. Because this meta-analysis does not include individual patient information, ethics committee approval was not needed.

### Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) stage III and IV gastric cancer diagnosis was histopathologically confirmed in patients; (2) hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) of PLR with survival outcomes including overall survival (OS) and/or progression-free survival (PFS) were reported, or the association between PLR and chemosensitivity of advanced gastric cancer was reported, or the association between PLR and clinicopathological characteristics of gastric cancer was reported; (3) a definite cut-off value of pretreatment PLR was determined; and (4) full-text articles published in English.

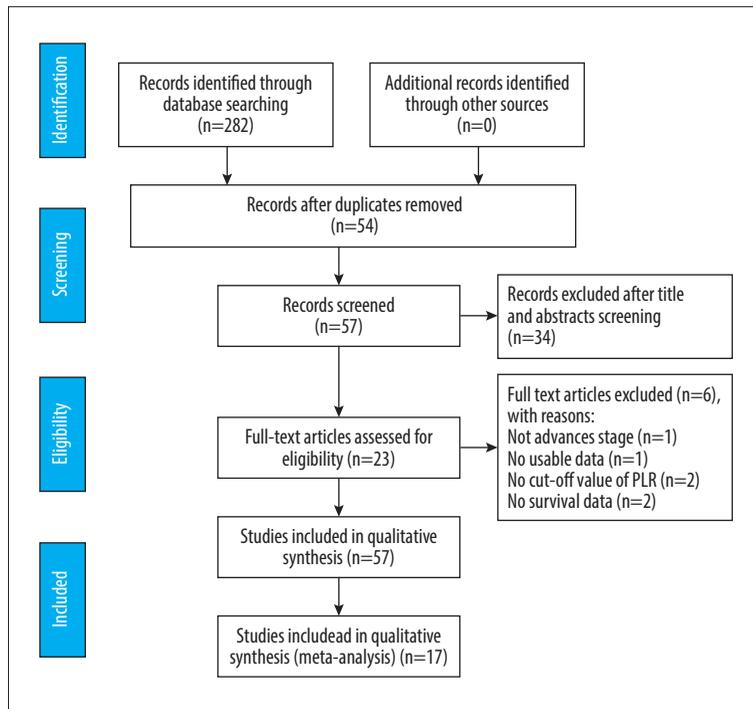
The exclusion criteria were as follows: (1) duplicate publications; (2) reviews, editorials, conference abstracts, letters and case reports; (3) basic research or animal studies; (4) studies without sufficient data.

### Outcome Assessment

Our primary outcome was the correlation between PLR and OS, DFS, and chemosensitivity in advanced GC patients. Secondary outcomes included the association between PLR and clinicopathological features in advanced GC patients.

### Data Collection and Quality Assessment

Studies assessing high PLR versus low PLR in predicting prognostic and chemosensitivity and survival of advanced gastric cancer patients were selected. Two investigators (WZ and BT) independently reviewed the articles retrieved in the literature search and extracted the relevant data. Any disagreements were



**Figure 1.** Flow chart of literature search and study selection.

resolved by discussion with a third reviewer (XP). The following data were independently collected from the retrieved articles by AH and RL: first author's name, publication year, study country, study period, number of cases, age, sex, time of follow-up, treatment, cut-off value of PLR, prognostic endpoints (OS or DFS), HRs with corresponding 95% CIs, chemosensitivity, and clinicopathological characteristics.

Quality assessment was performed in accordance with the Newcastle-Ottawa scale (NOS) [25]. The NOS scores range from 0 to 9, and if the score was higher than 6, the study was considered to be high-quality. Two reviewers (BT and MZ) independently calculated the NOS scores, and any disagreements were resolved by discussion with a third reviewer (RL). The study was independently examined by 3 investigators (XP, WZ, and AH). Any disagreements were resolved by discussion with a third reviewer (RL). All authors reviewed the manuscript, any disagreements were resolved by discussion to approve the final manuscript.

### Statistical Analysis

The pooled HRs and 95% CIs were used to assess the prognostic role of PLR on the survival (OS/DFS) of patients with advanced GC. HR >1 with  $P < 0.05$  indicated a poor prognosis in patients with high PLR. Statistical heterogeneity among studies was determined by using the Cochran Q-test and  $I^2$  test [26,27].  $I^2 > 50\%$  or  $P < 0.10$  were considered to indicate significant heterogeneity. A random-effects model was used if substantial heterogeneity was detected among studies; otherwise, a fixed-effects model was applied.

The subgroup analysis was performed by ethnicity, cut-off value, cut-off selection, sample size, treatment, and NOS score. The odd ratios (ORs) and 95% CIs were calculated to assess the correlations between PLR and clinicopathological features and chemosensitivity of patients with advanced GC. Sensitivity analysis was conducted to evaluate the reliability of the results. Publication bias was examined by using the Begg's test and Egger's test.  $P$  values  $< 0.05$  were considered statistically significant. All statistical analyses were performed using Stata version 12.0 (Stata Corporation, College Station, TX, USA).

## Results

### Search Results

The detailed selection process of literature selection is shown in **Figure 1**. A total of 282 records were identified after the initial literature search, and 225 duplicate articles were removed. After examining the title and abstract, 34 articles were discarded. Subsequently, the full text of the remaining 17 articles were evaluated, and 6 were discarded for the following reasons: 5 studies lacked necessary data and 1 study did not include advanced-stage patients. Finally, 17 studies comprising 3499 patients with advanced GC were finally identified in the meta-analysis [8,28-43].

### Characteristics of the Included Studies

The specific characteristics of 17 studies are summarized in **Table 1**. All selected studies were published between 2010

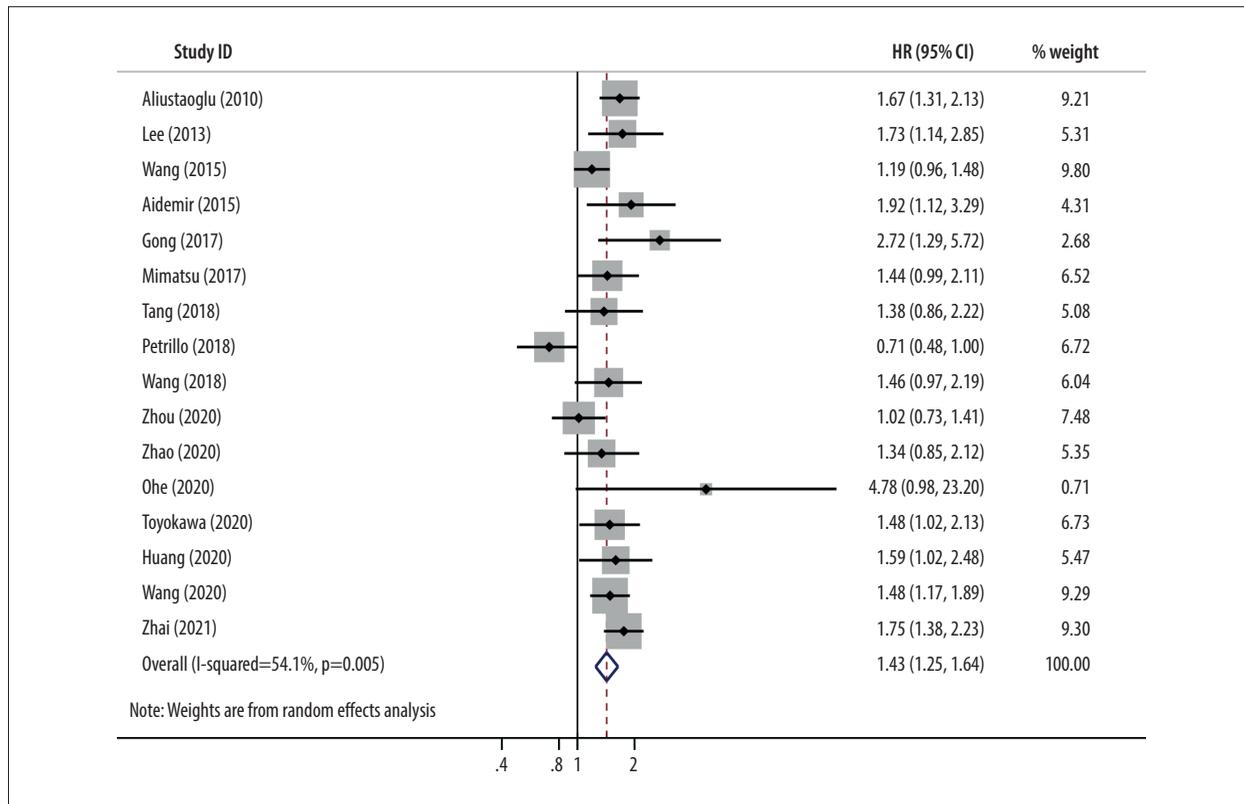
**Table 1.** Baseline characteristics of eligible studies for this meta-analysis.

Author	Year	Country	study design	Period	Patients n	Age (y) median (range)	Sex (M/F)
Aliustaoglu	2010	Turkey	Retrospective	2004-2008	168	60.1 (28-83)	114/54
Lee	2013	Korea	Retrospective	2007-2010	174	55 (24-74)	110/64
Wang	2015	China	Retrospective	2010-2011	120	68 (32-82)	75/45
Aidemir	2015	Turkey	Retrospective	2006-2013	50	65 (40-82)	30/20
Gong	2017	China	Retrospective	2007-2015	91	55 (26-70)	69/22
Mimatsu	2017	Japan	Retrospective	2006-2016	33	NA	27/6
Tang	2018	China	Retrospective	2010-2016	104	65 (31-78)	74/30
Petrillo	2019	Italy	Retrospective	2010-2017	151	62 (26-85)	97/54
Wang	2018	China	Retrospective	2005-2013	273	57	186/87
Zhou	2020	China	Retrospective	2010-2018	537	55 (25-83)	321/216
Zhao	2020	China	Retrospective	2012-2016	110	NA	84/26
Ohe	2020	Japan	Retrospective	2005-2018	41	65 (30-78)	34/7
Toyokawa	2020	Japan	Retrospective	1997-2012	225	68	114/111
Huang	2020	China	Retrospective	2008-2017	304	NA	198/106
Wang	2020	China	Retrospective	2010-2017	466	60 (20-88)	327/139
Gu	2020	China	Prospective	2013-2016	346	NA	NA
Zhai	2021	China	Retrospective	2007-2014	306	58 (28-85)	245/61

Author	Cut-off value	Cut-off selection	Treatment	Follow-up (m)	Survival analysis	NOS score
Aliustaoglu	160	NA	Chemotherapy	NA	OS	6
Lee	160	NA	Chemotherapy	14.9 (1-47.9)	OS, PFS	7
Wang	235	Median	Chemotherapy	40	OS	6
Aidemir	170	Median	Chemotherapy	NA	OS	7
Gong	161	ROC curve	Mixed	22 (8-67)	OS	8
Mimatsu	200	NA	Mixed	NA	OS	7
Tang	130.7	ROC curve	Mixed	NA	OS	7
Petrillo	157	Median	Chemotherapy	29 (20.4-37.5)	OS	8
Wang	210.6	ROC curve	Chemotherapy	NA	OS	7
Zhou	284	ROC curve	Chemotherapy	NA	OS, PFS	8
Zhao	143.39	ROC curve	chemotherapy	11.6	OS	8
Ohe	180	ROC curve	chemotherapy	NA	OS	7
Toyokawa	172	ROC curve	Mixed	80 (69-124)	OS	9
Huang	107.7	X-tile	Mixed	28.01 (1-99)	OS	8
Wang	174.79	Median	Chemotherapy	NA	OS, PFS	8
Gu	154	ROC curve	Mixed	50 (4-83)	DFS	7
Zhai	128	ROC curve	Mixed	11	OS	9

NA – not available; OS – overall survival; DFS – disease-free survival; NOS – Newcastle-Ottawa scale; ROC – receiver operating characteristics curve; PLR – platelet-to-lymphocyte ratio.



**Figure 2.** Forest plots for the association platelet to lymphocyte ratio and overall survival in patients with advanced gastric cancer (HR=1.429, 95% CI=1.246-1.639,  $P<0.001$ ). CI – confidence interval; HR – hazard ratio.

and 2021, and were conducted in 5 countries, including 1 in Italy [10], 1 in Korea [34], 2 in Turkey [31,32], 3 in Japan [29,39,42], and 10 in China [28,30,33,35-38,40,41,43]. There was only 1 prospective trail [40], and the sample sizes ranged from 33 to 537. The cut-off values for PLR in 17 studies ranged from 107.7 to 284. As for outcomes, 16 studies evaluated the association between PLR and OS [10,28-39,41-43], and 3 studies investigated the prognostic role of PLR in DFS [33,40,41]. Three studies investigated the association between the PLR and chemosensitivity [28-30], and 11 studies reported the correlation between the PLR and clinicopathological features [10,28,30,34,35,38-43]. In addition, the NOS scores of the quality of 17 included studies ranged from 6 to 9, indicating high quality.

### Overall Quality of the Included Studies

The Newcastle-Ottawa Scale was used to assess the quality of all the included studies. The NOS scores of the quality of 17 included studies ranged from 6 to 9, indicating high quality.

### Correlation Between PLR and OS in Advanced GC Patients

Sixteen studies containing 3153 patients with advanced GC evaluated the prognostic value of PLR in OS [10,28-39,41-43].

As shown in **Figure 2**, moderate heterogeneity existed among the included studies, so a random-effects model was used ( $I^2=54.1%$ ,  $P=0.05$ , **Figure 2 and Table 2**). The median score was used as the cut-off value to categorize low or high PLR. The pooled HRs and 95% CIs demonstrated that patients with a high PLR were associated with poor OS in advanced GC (HR=1.429, 95% CI=1.246-1.639,  $P<0.001$ ).

### Subgroup Analysis of Correlation Between PLR and OS

Due to the moderate heterogeneity, we performed subgroup analyses to minimize the impact of differences among studies on the pooled results. Subgroup analysis was introduced for further investigation, stratified by ethnicity, cut-off value, cut-off selection, sample size, treatment, and NOS score. The data showed that there were significant correlations between high PLR and sample size, treatment, cut-off value, and NOS score (**Table 2**).

### Correlation Between PLR and DFS in Advanced GC Patients

Three clinical studies investigated the association between PLR and DFS in resected GC [33,40,41]. Pooled results demonstrated that high PLR was correlated to poor DFS (HR=1.47, 95% CI=1.14-1.88,  $P=0.003$ ) compared with low PLR in patients

**Table 2.** Subgroup analyses of pooled HRs and 95% CIs for OS based on different factors.

Subgroup analysis	No. of studies	No. of patients	Effects model	HR (95% CI)	P value	Heterogeneity	
						I <sup>2</sup> (%)	p value
OS							
NOS score							
>7	9	2190	Random	1.36 (1.08-1.72)	0.010	70.8	0.001
≤7	7	963	Fixed	1.46 (1.29-1.65)	<0.001	16.1	0.303
Sample size							
≥168	8	2453	Fixed	1.53 (1.37-1.70)	<0.001	15.5	0.308
<168	8	700	Random	1.37 (1.05-1.80)	0.020	64.1	0.007
Treatment							
Chemotherapy	10	2090	Random	1.34 (1.11-1.62)	0.002	63.7	0.003
Mixed	6	1063	Fixed	1.62 (1.39-1.89)	<0.001	0.0	0.646
Cut-off value							
≥161	9	1836	Fixed	1.37 (1.22-1.53)	<0.001	37.3	0.120
<161	7	1317	Random	1.41 (1.11-1.80)	0.005	68.6	0.004
Cut-off method							
ROC curve	8	1687	Fixed	1.48 (1.29-1.71)	<0.001	41.7	0.100
Median	4	787	Random	1.22 (0.88-1.70)	0.238	78.0	0.003
NA	3	375	Fixed	1.62 (1.34-1.95)	<0.001	0.0	0.774
X-title	1	304	–	1.59 (1.02-2.48)	0.041	–	–
Ethnicity							
Caucasian	3	369	Random	1.30 (0.71-2.39)	0.394	87.8	<0.001
Asian	13	2784	Fixed	1.43 (1.30-1.58)	<0.001	25.1	0.190
Total	16	3153	Random	1.43 (1.25-1.64)	<0.001	54.1	0.005

CI – confidence interval; HR – hazard ratio; OS – overall survival; DFS – disease-free survival; ROC – receiver operating characteristics curve; PLR – platelet to lymphocyte ratio (I<sup>2</sup> >50% or P<0.10 were considered to indicate significant heterogeneity, random-effects model was used; otherwise, a fixed-effects model was applied.)

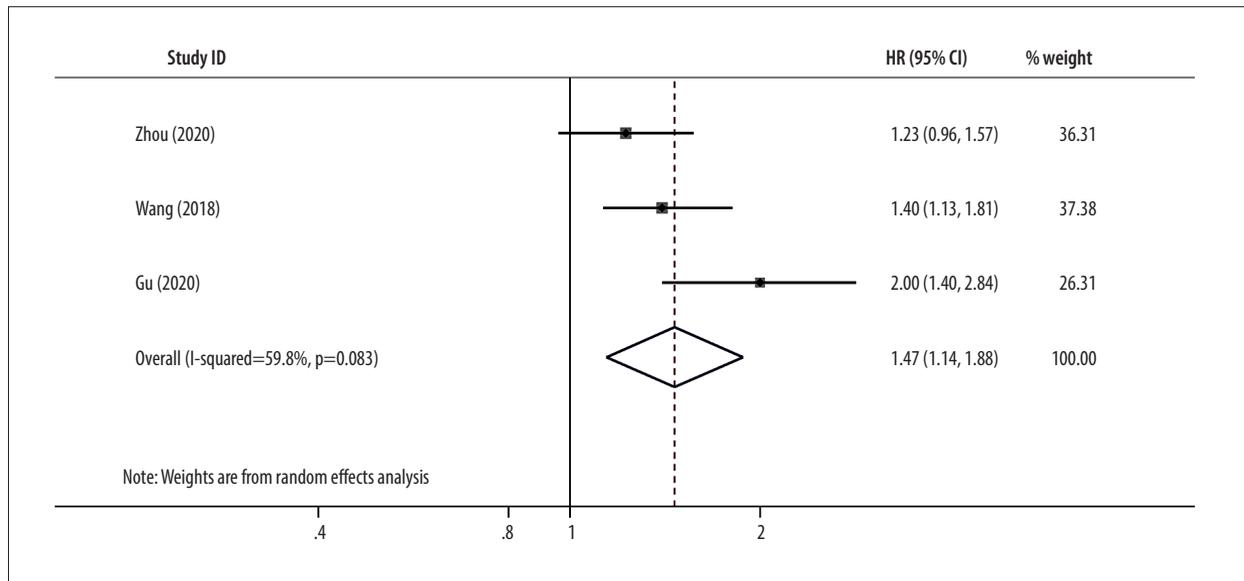
with advanced GC. As shown in **Figure 3**, a random-effects model was applied for analysis due to moderate heterogeneity (I<sup>2</sup>=59.8%, P=0.083).

**Subgroup Analysis of Correlation Between PLR and DFS**

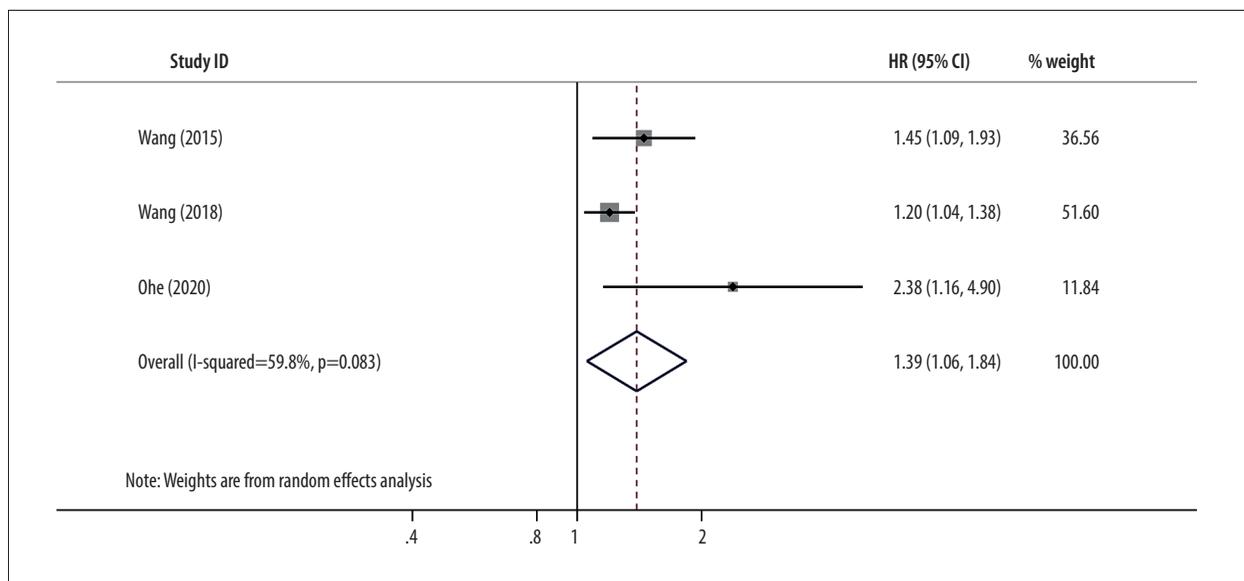
Similar to the OS, subgroup analysis revealed that there was significant correlation between high PLR and ethnicity, sample size, and NOS score (**Table 2**).

**Association Between PLR and Chemosensitivity**

The association between the PLR and chemosensitivity was analyzed from 3 studies [28-30]. As shown in **Figure 4**, moderate heterogeneity existed among the included studies, so a random-effects model was used (I<sup>2</sup>=59.8%, P=0.083 **Figure 4**). The analysis revealed that low PLR was associated with a higher response to chemotherapy in patients with advanced GC (OR=1.395, 95% CI=1.056-1.841, P=0.019).



**Figure 3.** Forest plots for the association platelet to lymphocyte ratio and disease-free survival in patients with advanced gastric cancer (HR=1.47, 95% CI=1.14-1.88,  $P=0.003$ ). CI – confidence interval; HR – hazard ratio.



**Figure 4.** Forest plots of the correlation between platelet to lymphocyte ratio and chemosensitivity in advanced gastric cancer (OR=1.395, 95% CI=1.056-1.841,  $P=0.019$ ).

### Association Between PLR and Clinicopathological Features

To evaluate the associations between PLR and clinicopathological features of GC, we identified 6 clinical features. The features included sex (male versus female), age (years) ( $\geq 60$  versus  $< 60$ ), tumor differentiation (poor versus moderate/well-differentiated), tumor size ( $\geq 5$  cm versus  $< 5$  cm), CEA ( $\geq 5$  versus  $< 5$ ), and ECOG ( $\geq 2$  versus  $< 2$ ) (Table 3 and Figure 5). However, there was no significant correlation between PLR and clinicopathological features, sex (OR=0.940, 95% CI=0.794-1.112,  $P=0.468$ ), age (OR=1.398, 95% CI=0.827-2.362,  $P=0.211$ ), tumor

differentiation (OR=0.985, 95% CI=0.902-1.075,  $P=0.734$ ), tumor size (OR=1.130, 95% CI=0.567-2.253,  $P=0.729$ ), CEA (OR=1.128, 95% CI=0.965-1.320,  $P=0.131$ ), or ECOG (OR=1.355, 95% CI=0.492-3.731,  $P=0.557$ ).

### Sensitivity Analysis

Sensitivity analysis was conducted to evaluate the stability of pooled HRs for OS and DFS. As shown in Figure 6, the sensitivity analysis demonstrated the credibility of the results of this meta-analysis.

**Table 3.** Correlations of PLR and clinicopathological characteristics in patients with advanced GC.

Clinicopathological features	No. of studies	No. of patients	Effects model	OR (95% CI)	P value	Heterogeneity	
						I <sup>2</sup> (%)	p value
ECOG (≥2 versus <2)	4	567	Random	1.36 (0.49-3.73)	0.557	53.1	0.094
Tumor size (≥5 cm versus <5 cm)	3	557	Random	1.13 (0.57-2.25)	0.729	85.6	0.001
Sex (Male versus Female)	12	1989	Random	0.94 (0.79-1.11)	0.468	84.2	<0.001
Age (years) (≥60 versus <60)	4	1077	Random	1.40 (0.83-2.36)	0.211	94.5	<0.001
Tumor differentiation (poor versus moderate/well)	7	1428	Fixed	0.99 (0.90-1.08)	0.734	0.0	0.454
CEA leve (≥5 versus <5)	5	1129	Fixed	1.13 (0.97-1.32)	0.131	0.0	0.635

CI – confidence interval; OR – odds ratio; PLR – platelet-to-lymphocyte ratio; GC – gastric cancer; ECOG – Eastern Cooperative Oncology Group, CEA – carcino-embryonic antigen.

**Publication Bias**

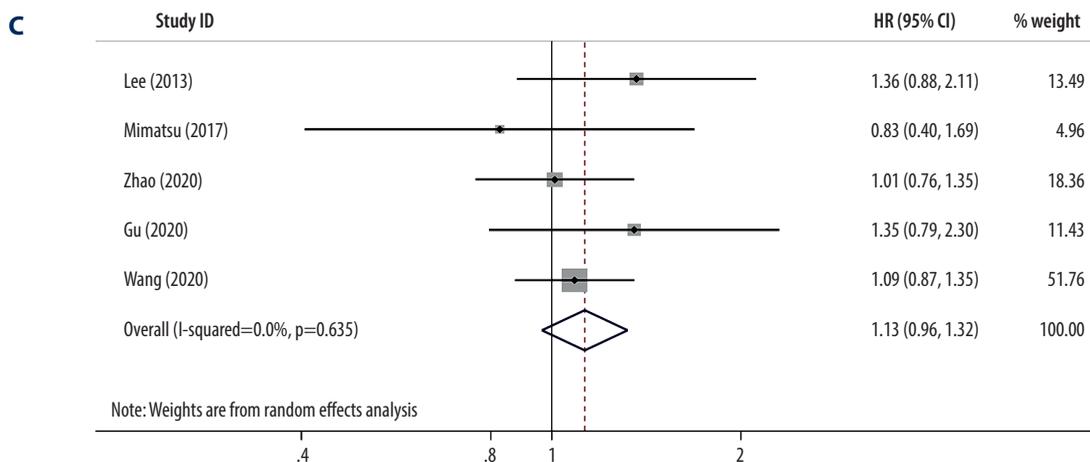
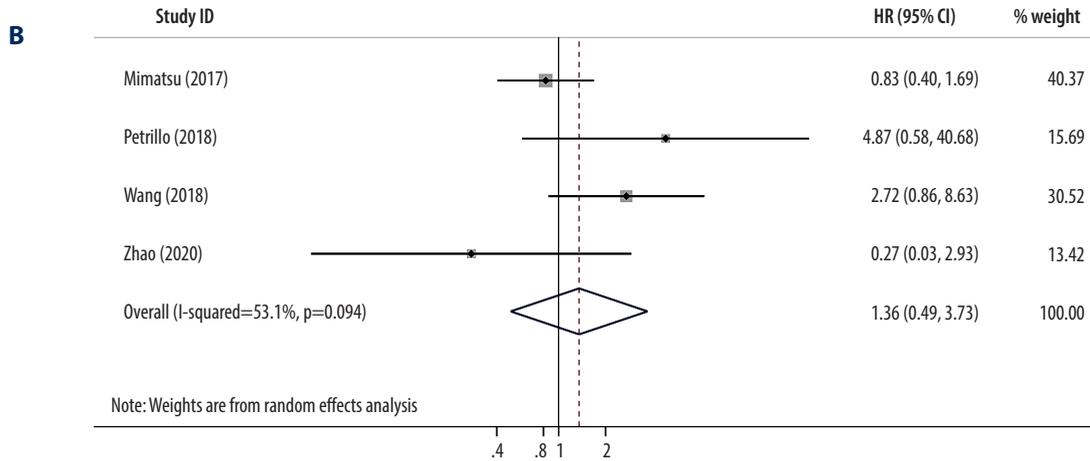
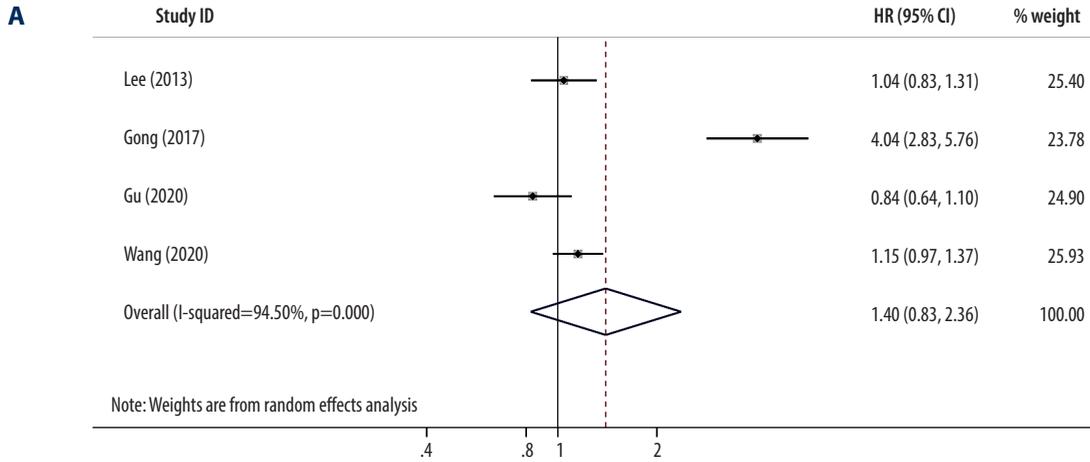
The Begg’s funnel and Egger’s test were used to estimate the potential publication bias. The results showed that there was no significant bias for OS (Begg’s p=0.260, Egger’s p=0.346) or PFS (Begg’s P=1.000, Egger’s P=0.288) (Figure 7).

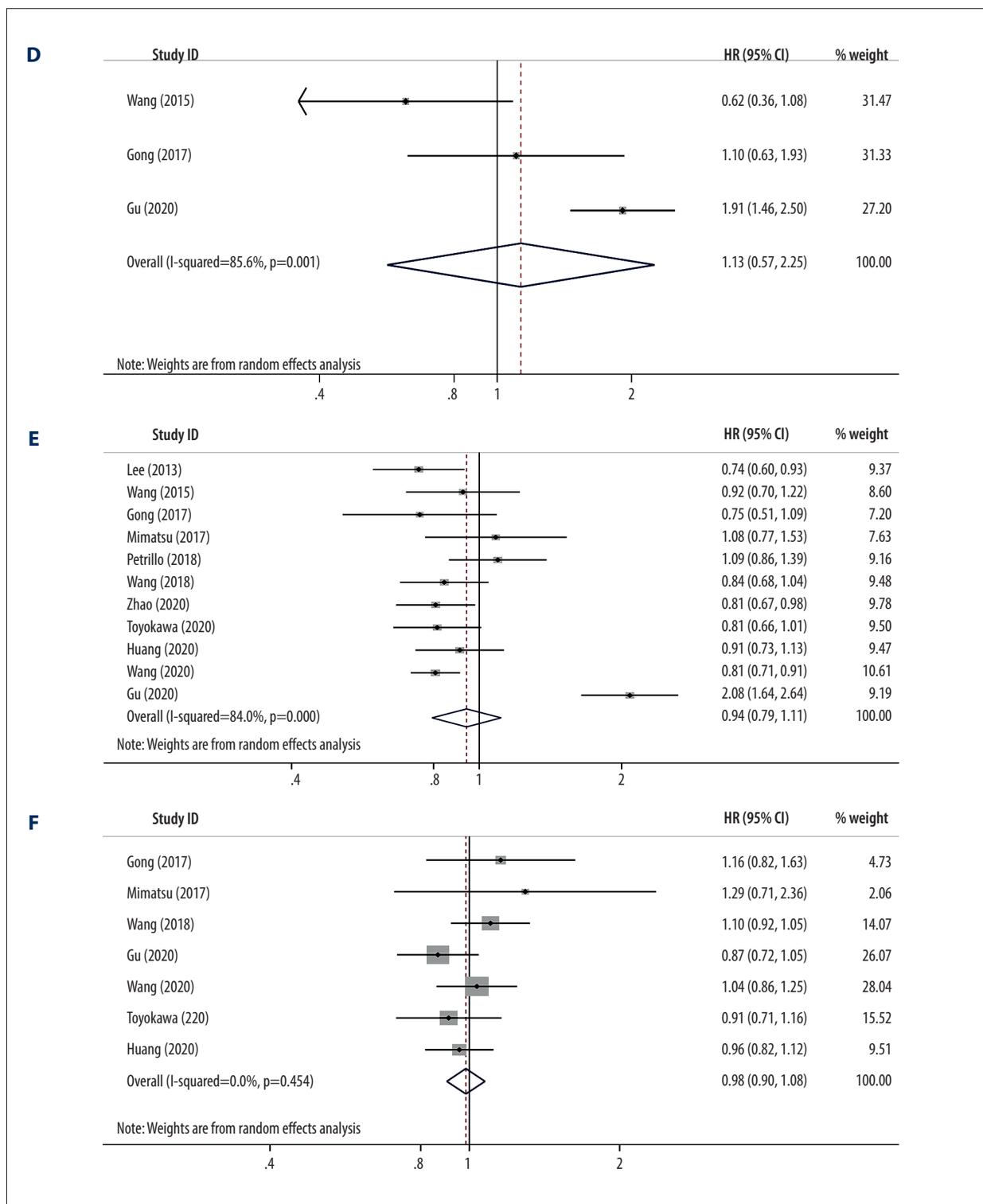
**Discussion**

Several studies have reported the association between PLR and the prognosis of gastric cancer, but they yielded conflicting results, and these studies including many early-stage GC patients [21,22,44,45]. Thus, the prognostic value of the PLR remains unclear in advanced GC, and there have no study in predictor of chemosensitivity value of PLR for advanced GC. Therefore, we conducted this meta-analysis to evaluate the ability of PLR to predict prognosis and chemosensitivity in patients with advanced GC. Based on the available data (N=3499), the results of the present meta-analysis have some clinical implications. Our meta-analysis demonstrated that higher PLR was associated with worse OS, PFS, and chemosensitivity in patients with advanced GC. Moreover, the association of an elevated PLR with OS remained substantial in studies with heterogeneous sample sizes, treatments, cut-off values, and NOS scores. However, we did not find a significant correlation between PLR and clinicopathological features in patients with advanced GC. As the PLR is a blood-derived parameter that is inexpensive and readily available, it could be routinely used to assess disease progression and chemosensitivity in patients with advanced GC. The results of our study may assist in predicting cancer prognosis, and, more importantly, help develop optimal treatment strategies.

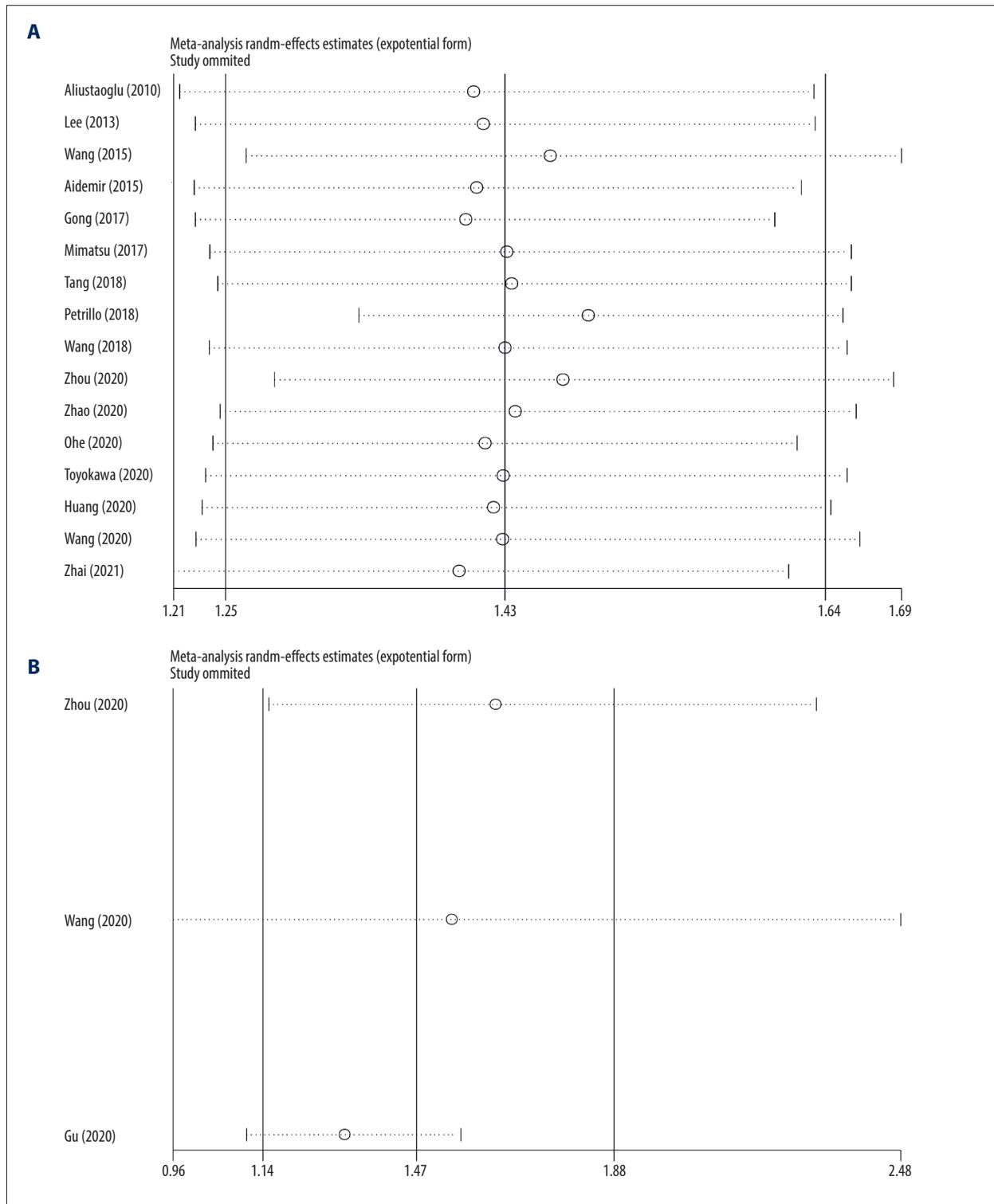
PLR is based on peripheral platelet and lymphocyte counts. A high PLR corresponds to high platelet and/or low lymphocyte counts. The interplay between inflammatory responses and tumor invasion may suggest a possible explanation. Platelets are involved in the tumorigenesis and metastasis of cancer cells by secreting tumor growth factors [46]. Lymphocytes are an important component of the immune system and play a vital role in the suppression of tumor progression [47]. Based on the above evidence, it is reasonable to speculate that a normal range of PLR signifies the balance between the degree of tumor progression and the status of anti-tumor immunity. High PLR represents elevated platelets or decreased lymphocytes, implying the weakened anti-tumor immune response and rapid deterioration. Hence, it is reasonable that high PLR predicts unfavorable OS and DFS in advanced GC.

Systemic inflammation and tumor microenvironments play an important role in modulating chemotherapy resistance [48-50]. The association of high PLR with low chemotherapeutic efficacy could result from an elevated platelet count and/or a decreased lymphocyte count. Activated platelets create a pro-coagulant microenvironment that allows tumor cells to coat themselves with platelets and escaped the patients’ immune system [51]. It was shown that overexpression of TGF-β receptor 2 (TGFB2) decreased 5-fluorouracil sensitivity of GC cells [52]. VEGF-C mediated cisplatin resistance in GC cells, while microRNA-101 that targeted VEGF-C could reverse the resistance [53]. It was reported that the expression of ERCC1 and GSTM1 positive genotype is predictive of chemotherapy treatment outcome in patients with advanced gastric cancer [54,55], but none of these factors is currently used clinically because they are invasive, required specific laboratory equipment and complex methodology. PLR has the advantages of

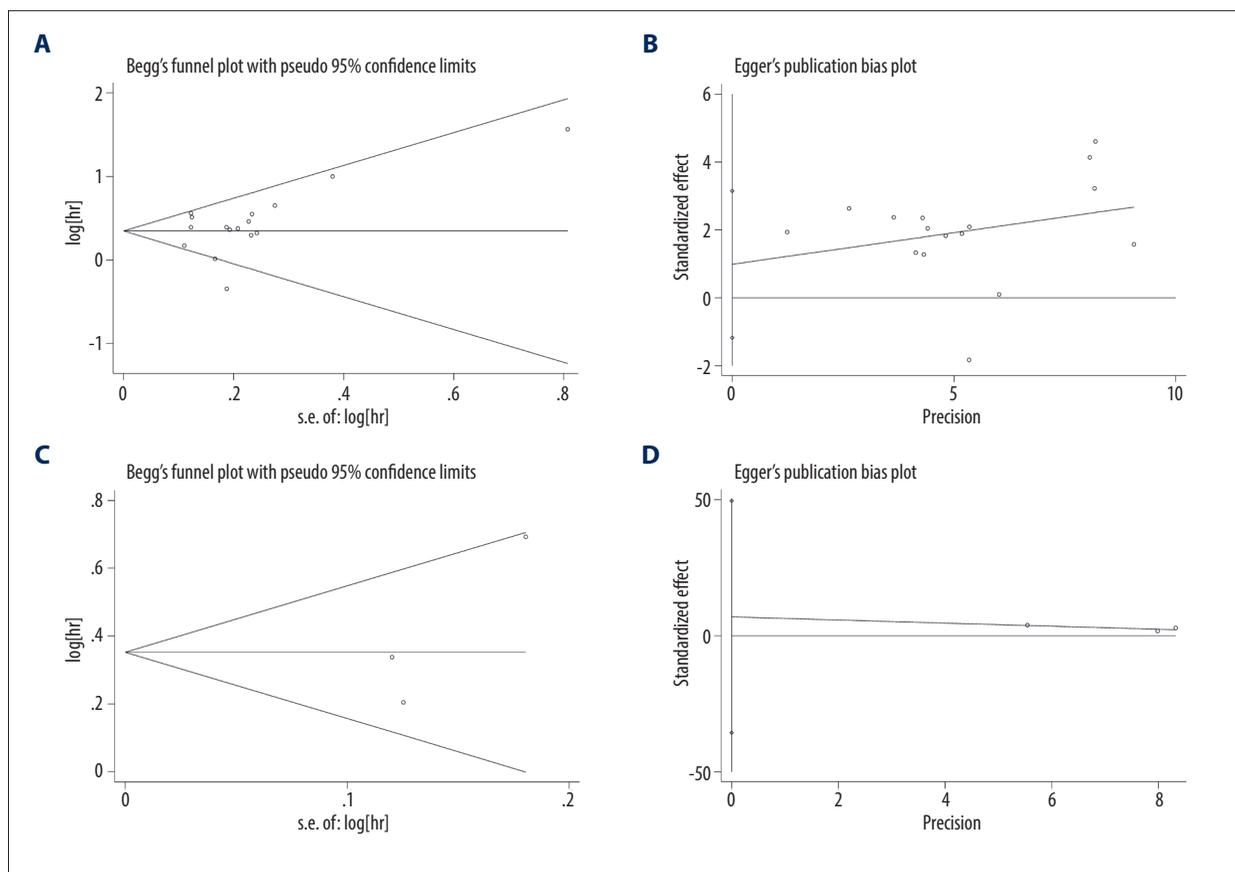




**Figure 5.** Forest plots of the correlation between platelet-to-lymphocyte ratio and clinical features in advanced gastric cancer. **(A)** Age (years) ( $\geq 60$  versus  $< 60$ , OR=1.398, 95% CI=0.827-2.362,  $P=0.211$ ); **(B)** ECOG ( $\geq 2$  versus  $< 2$ , OR=1.355, 95% CI=0.492-3.731,  $P=0.557$ ); **(C)** CEA ( $\geq 5$  versus  $< 5$ , OR=1.128, 95% CI=0.965-1.320,  $P=0.131$ ); **(D)** Tumor size ( $\geq 5$  cm versus  $< 5$  cm, OR=1.130, 95% CI=0.567-2.253,  $P=0.729$ ); **(E)** Sex (male versus female, OR=0.940, 95% CI=0.794-1.112,  $P=0.468$ ); **(F)** Tumor differentiation (poor versus moderate/well, OR=0.985, 95% CI=0.902-1.075,  $P=0.734$ ).



**Figure 6.** Sensitivity analysis for the association between platelet-to-lymphocyte ratio with survival in advanced gastric cancer. (A) Overall survival, (B) Disease-free survival.



**Figure 7.** Publication bias assessed by Begg's test and Egger's test. (A) Begg's test the publication bias for overall survival,  $P=0.260$ ; (B) Egger's test for overall survival,  $P=0.346$ ; (C) Begg's test the publication bias for ratio (disease-free survival,  $P=1.000$ ); (D) Egger's test for disease-free survival,  $P=0.288$ .

simplicity, convenience, affordability, and reproducibility, and it may be helpful for guiding treatment and monitoring treatment efficacy.

Although we performed this meta-analysis according to the PRISMA guidelines, this meta-analysis still has several limitations. First, no randomized controlled trials were enrolled in this study and almost all included studies were retrospective, which may have caused some heterogeneity and higher  $I^2$  when integrated. Second, the cut-off value of PLR was not uniform among the included studies, which might be the main source of the substantial heterogeneity and higher  $I^2$ . Third, 1 HR was extracted from univariate analyses, and may have overestimated effect sizes. In addition, only 3 studies assessed the ability of PLR to predict DFS and chemosensitivity, and this may have reduced the accuracy of the correlation between PLR and DFS and chemosensitivity. Prospective studies on this topic are needed.

## Conclusions

Our study revealed that high pretreatment PLR was obviously associated with unfavorable OS, PFS, and chemosensitivity in patients with advanced GC. These results indicate that pretreatment PLR could be an easily accessible and cost-effective prognostic and clinical decision-making biomarker for advanced GC in clinical practice.

## Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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