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Inflammation and nutrition-based biomarkers in the prognosis of oesophageal cancer: a systematic review and meta-analysis

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ABSTRACT

Background Accumulating literature has shown the predictive values of inflammation and nutrition-based biomarkers in the prognosis of oesophageal cancer but with inconsistent findings.

Method We performed a meta-analysis to systematically evaluate the predictive value of the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), C reactive protein-to-albumin ratio (CAR), systemic inflammation index (SII), prognostic nutritional index (PNI), Glasgow Prognostic Score (GPS) and modified Glasgow Prognostic Score (mGPS) in oesophageal cancer. The outcome indicators include the overall survival (OS), disease-free survival (DFS) and cancer-specific survival (CSS). We applied pooled HR, sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, diagnostic odds ratio and area under the curve together with 95% CI to estimate the predictive accuracy.

Results A total of 72 studies, including 22 260 patients, were included in the meta-analysis. Elevated NLR, PLR CAR, SII, GPS, mGPS and decreased LMR and PNI were associated with poor OS of oesophageal cancer. A high level of NLR, PLR and GPS was related to poor DFS. A high level of NLR and GPS was related to poor CSS. The summarised AUC of CAR (0.72, 95% CI: 0.68 to 0.75) and mGPS (0.75, 95% CI: 0.71 to 0.78) surpassed any other indicators.

Conclusions Clinical indicators such as NLR, PLR, LMR, PNI, SII, CAR, GPS and mGPS have the moderate predictive ability in OS, DFS and CSS of oesophageal cancer. The pretreatment level of CAR and mGPS showed an outstanding prediction value in 5-year OS for oesophageal cancer.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We used internationally recognised critical assessment tools to assess the quality of individual studies.
⇒ The pooled results were stable due to the large sample size.
⇒ The prognostic performance of biomarkers for oesophageal cancer was systematically compared for the first time.
⇒ Different cut-off values may result in heterogeneity and bias.
⇒ Heterogeneity was not fully explained.

BACKGROUNDS

Globally, oesophageal cancer is the seventh most common cancer and the sixth leading cause of cancer death.[1] In 2020, there were 570 000 new cases of oesophageal cancer and about 500 000 deaths worldwide.[2] Pathologically, squamous cell carcinoma (SCC) and adenocarcinoma are the major histological types. Oesophageal adenocarcinoma is mainly observed in industrialised countries, and nearly half of the cases occur in Northwest Europe and North America, while oesophageal squamous cell carcinoma (ESCC) is more common in China, Central Asia or South Africa. Despite substantial efforts in diagnosis, accurate staging and advanced treatments, the 5-year survival rate remains unfavourable with frequent metastasis and recurrence.[3] The pathological tumor-node-metastasis (TNM) stage is the gold standard for predicting oncological outcomes after surgery.[4] However, with the diversification of treatment methods and the complexity of prognostic factors, prognosis prediction tends to be unsatisfactory. Therefore, it is urgent to find better prognostic biomarkers to guide clinical treatment and appropriate follow-up.

Increasing evidence indicates that systemic inflammatory response and nutritional status are involved in tumour development and influence the clinical prognosis. Principal inflammation-based prognostic scores[5–7] include a neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), C reactive protein-to-albumin ratio (CAR), systemic inflammation index (SII), pretreatment

albumin levels and lymphocyte to monocyte ratio. Typical nutrition-based prognostic scores[8 9] are prognostic nutritional index (PNI) based on serum albumin and total lymphocyte count, Glasgow Prognostic Score (GPS) based on elevated C reactive protein (CRP) concentration and low levels of albumin and modified Glasgow Prognostic Score (mGPS), a modified version of GPS. Recently, accumulating literature has shown the prognostic values of these inflammation and nutrition-based prognostic markers in oesophageal cancer, but with inconsistent findings. Hence, it is meaningful to distinguish an accurate prognosis index for patients with oesophageal cancer to guide individualised therapy and precision service.

In the current study, we performed a systematic review of relevant literature. We applied the meta-analysis to explore the accuracy of inflammation and nutrition-based prognostic scores for patients with oesophageal cancer.

MATERIALS AND METHODS

Literature search

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Two students (YJ and DX) independently searched PubMed, Web of Science and Cochrane Library Databases for eligible articles from the inception of databases to March 2020. Additionally, references in the eligible publications were also reviewed for potential studies. The language was limited to English. The search terms are listed in online additional file 1. The detailed search procedure is illustrated in figure 1.

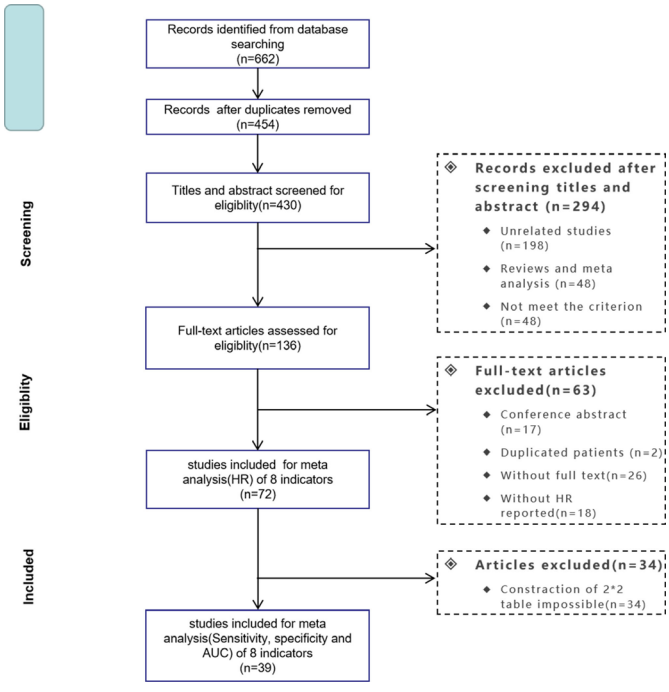

Figure 1 Flow diagram of the search process. AUC, area under the curve

The definition of outcome

Overall survival (OS) was defined as the time from the beginning of treatment to the death due to all causes or last follow-up. Cancer-specific survival (CSS) was defined as the time from the beginning of therapy to the time of cancer-related death. Disease-free survival (DFS) was defined as the time from the start of treatment to the cancer recurrence or the occurrence of the second primary malignancy.[10]

Selection criteria

Articles were included if they met the following criteria: (1) patients were histopathologically confirmed to be primary oesophageal cancer; (2) prognostic indicators were measured before esophagectomy, chemotherapy or radiotherapy; (3) hazard ratios (HRs) with 95% CIs were reported in multivariate analysis. Studies were excluded if they were: (1) reviews, case reports, letters or conference abstracts; (2) studies with insufficient data; or (3) duplicate publications.

Data extraction

For each study, the following information was extracted by two students (YJ and DX): the name of the first author, year of publication, country, study design, pathological type, number of patients, age, sex, end-point, follow-up time, cut-off selection, therapy, tumour stage, cut-off values and HRs (95% CIs). We further collected the data of true-positive (TP), false-positive (FP), true-negative (TN) and false-negative (FN) for 5-year OS directly provided in the paper or calculated by comparable data (the number of people in the high-risk and low-risk groups according to the cut-off values and the corresponding number of deaths and survivors). If only the area under the curve (AUC) was reported, we contacted the corresponding author for original data. If we could not get a response, we only included this study in the first part of the analysis.

Quality assessment

Two reviewers (HS and BQ) independently assessed the methodological quality of the studies using the Quality Assessment of Diagnostic Accuracy Studies 2 tool.[11] Each item was judged as 'yes', 'no' or 'unclear'. Any signalling question answered 'yes' indicated a low risk of bias, while 'no' showed a high risk of bias. If the answer was uncertain, the domain was judged as having an uncertain risk of bias.

Statistical analysis

The risk of bias was analysed and plotted using Review Manager V.5.3 (London, UK). The meta-analysis was performed using STATA V.15.0 (Texas, USA). The strength of NLR, PLR, LMR, PNI, SII, CAR, GPS, mGPS in association with OS, CSS and DFS was measured by the combined HRs and their 95% CIs. Cochran's Q test and Higgins I^2 statistics were undertaken to assess the heterogeneity of studies. If $p \geq 0.10$ in the Q test or $I^2 < 50\%$, we used the fixed-effect model; otherwise, we used the random-effect model. Publication bias was assessed by

Begg and Egger test. The sensitivity analysis was utilised by omitting individual study one-by-one to evaluate the robustness of the results. All p values were two-tailed, and a p value <0.05 was considered statistically significant.

The pooled sensitivity, specificity, AUC and the corresponding 95% CI were calculated by TP, FP, FN and TN using a bivariate regression model. The threshold effects were calculated by testing the Spearman correlation using Meta-DiSc (Madrid, Spain).[12] If $I^2 \geq 50\%$ and p value ≤0.05, the heterogeneity was significant due to the non-threshold effect, and then we used the meta-regression analysis to find the source of heterogeneity. The pooled positive likelihood ratio (P-LR), negative likelihood ratio (N-LR) and diagnostic odds ratio (DOR) were also calculated to understand the performance of the prognostic index better. Deek's funnel plot was used to detect publication bias. To evaluate the difference of AUC between biomarkers, we checked the overlap of 95% CIs. If not, we used the following *z*-test $((X_1-X_2)/(SE_1^2+SE_2^2)^{1/2})$, where X_1 and X_2 represented the indicators, and SE_1 and SE_2 were the corresponding standard errors.[13] It was considered significantly different if the p value obtained from the z-test was less than P′ ($0.05/n$, n was the number of comparisons). The comparison for sensitivity, specificity, P-LR, N-LR, or DOR was also performed.

RESULTS

Literature selection and study characteristics

The initial search identified 662 potentially relevant records. After removing duplicates and papers that did not meet the inclusion criteria, 72 studies with 22 260 subjects remained for the systematic review (online additional file 2). A flowchart demonstrating the process of study selection is illustrated in figure 1. Most studies were carried out in Asia (42 in China; 23 in Japan). Before treatment, the blood cell counts used to calculate NLR, PLR, LMR and CAR were obtained. The baseline characteristics and treatment methods are presented in online additional file 2.

Risk-of-bias and quality assessments

Figure 2 illustrates the risk assessment of bias. A high risk of selection bias was observed in all studies. Nearly one-third of the studies had an unclear bias in study attrition. One study had an unclear bias for detection bias, and two studies had the risk of bias in measuring prognostic factors and outcomes, respectively. Six studies were judged as having an unclear performance bias.

Prognostic indicators in OS, DFS and CSS of esophageal cancer

As shown in figure 3 (A–H), factors significantly contributing to a short OS were a high level of NLR (HR: 1.43, 95% CI: 1.30 to 1.58, p<0.001; I^2=61.7%, p_{het} <0.001), PLR (HR: 1.26, 95% CI: 1.18 to 1.35, p<0.001; I^2=29.8%, p_{het}=0.108), CAR (HR: 1.84, 95% CI: 1.60 to 2.10, p<0.001; I^2=41.8%, p_{het}=0.079), SII (HR: 1.46, 95% CI: 1.30 to 1.65, p<0.001; I^2=41.0%, p_{het}=0.118), GPS (HR: 2.35, 95% CI: 1.99 to 2.76, p<0.001; I^2=36.5%, p_{het}=0.078) or mGPS (HR: 1.69, 95% CI: 1.49 to 1.92, p<0.001; I^2=48.4%, p_{het}=0.022), and low level of LMR (HR: 1.37, 95% CI: 1.14 to 1.65, p=0.001; I^2=84.9%, p_{het} <0.001) and PNI (HR: 1.51, 95% CI: 1.36 to 1.68, p<0.001; I^2=45.8%, p_{het}=0.048).

Patients with an elevated NLR (HR: 1.21, 95% CI: 1.04 to 1.41, p=0.011; I^2=43.4%, p_{het}=0.089) and GPS (HR: 1.64, 95% CI: 1.33 to 1.94, p<0.001; I^2=45.5%, p_{het}=0.119) had a worse CSS (figure 3I–J) .

NLR (HR: 1.39, 95% CI: 1.10 to 1.75, p=0.005; I^2=60.9%, p_{het}=0.018), PLR (HR: 1.30, 95% CI: 1.12 to 1.51, p<0.001; I^2=33.0%, p_{het}=0.202) and GPS (HR: 2.44, 95% CI: 1.28 to 4.66, p<0.007; I^2=57.5%, p_{het}=0.052) were negatively correlated with DFS. No significant association was found for LMR (HR: 1.08, 95% CI: 0.85 to 1.38, p=0.522; I^2=79.8%, p_{het}<0.001) (figure 3K–N).

Subgroup analysis and meta-regression

Subgroup analysis and meta-regression were further conducted according to the cut-off value, sample size, follow-up time, sex, age, clinical stage and region (online additional file 3). The heterogeneity of OS studies was relatively low except LMR (I^2=84.9%) and NLR (I^2=61.7%). The pooled HR was significantly different between studies with more or less than 280 patients, indicating that the sample size may be the source of heterogeneity for LMR. Similarly, we found the source of heterogeneity for other indicators. The follow-up time may be the source of heterogeneity for PLR (p=0.004) and GPS (p=0.027). The sample size may be the source of heterogeneity for SII (p=0.047) and mGPS (p=0.014). The sex ratio may be the source of heterogeneity for CAR (p=0.045). In DFS analysis, we found that cut-off value and region may be the source of high heterogeneity of LMR (p=0.034) and NLR (p=0.018), respectively.

Publication bias

Begg and Egger's tests were applied to estimate the publication bias. As shown in online additional file 3, no significant publication bias was observed.

Sensitivity analysis

We performed a sensitivity analysis by excluding one study each time. As shown in online additional 4, the results were not substantially changed, demonstrating the reliability and stability of the current meta-analysis.

Pooled sensitivity, specificity, DOR, and AUC of indicators

We further extracted TP, FP, FN and TN from each study (online additional file 2) to calculate the pooled accuracy of each indicator for a 5-year OS. There were 11 studies for NLR, 11 studies for PLR, 7 studies for LMR, 6 studies for CAR, 6 studies for SII, 7 studies for PNI, 6 studies for GPS and 5 studies for mGPS.

Threshold effect

The Spearman correlation coefficient (p value) for NLR, PLR, LMR, PNI, SII, CAR, GPS and mGPS was 0.56

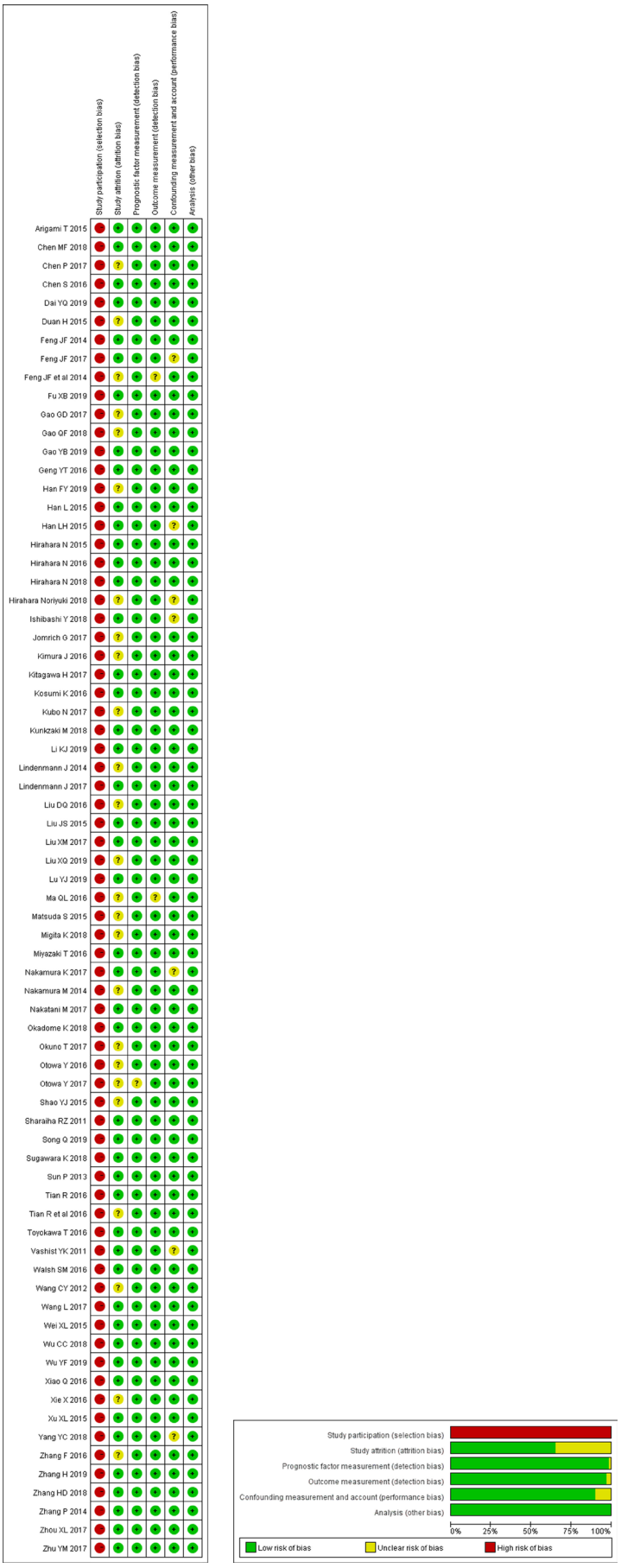

Figure 2 Risk of bias and applicability concerns.

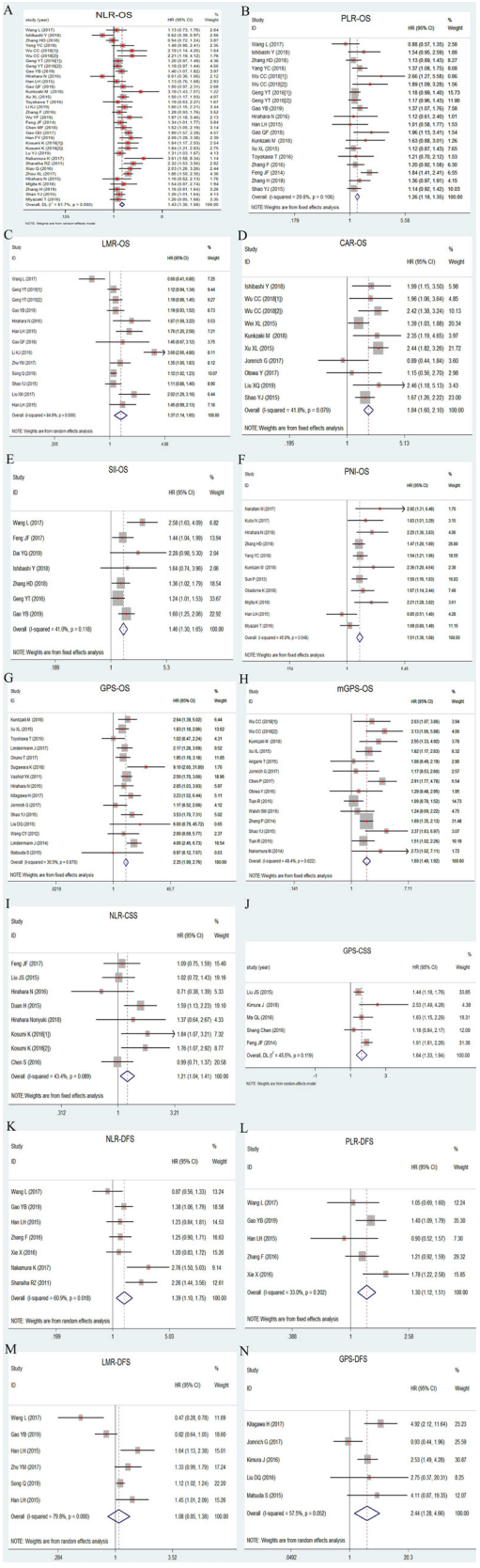

Figure 3 Forest plot of HR for 5- year OS, DFS and CSS in patients with oesophageal cancer. (A) NLR-OS; (B) PLR-OS; (C) LMR-OS; (D) CAR-OS; (E) SII-OS; (F) PNI-OS; (G) GPS-OS; (H) mGPS-OS; (I) NLR-CSS; (J) GPS-CSS; (K) NLR-DFS; (L) PLR-DFS; (M) LMR-DFS; (N) GPS-DFS. CAR, C reactive protein-to-albumin ratio; CSS, cancer-specific survival; DFS, disease-free survival; GPS, Glasgow Prognostic Score; LMR, lymphocyte-to-monocyte ratio; mGPS, modified Glasgow Prognostic Score; NLR, neutrophil-to-lymphocyte ratio; OS, overall survival; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index; SII, systemic inflammation index.

(0.07), 0.59 (0.06), 0.57 (0.18), 0.75 (0.05), 0.77 (0.07), 0.20 (0.70), 0.77 (0.07) and −0.10 (0.87), respectively, indicating no significant threshold effect.

Forest plot and subgroup analysis

Forest plots of sensitivity and specificity are shown in figure 4. SII had the highest pooled sensitivity (0.61, 95% CI: 0.48 to 0.73), while CAR (0.84, 95% CI: 0.71 to 0.91) had the highest pooled specificity. The I^2 of the sensitivity and specificity of these prognostic indicators were relatively high (around 70%–90%) except GPS (sensitivity: 43.76%; specificity: 6.96%). We further conducted a subgroup analysis and meta-regression (online additional file 5). For SII, the sensitivity of studies with a cut-off level ≥410 ng/mL (0.47, 95% CI: 0.37 to 0.57) was significantly lower than the studies with a cut-off level <410 ng/mL (0.73, 95% CI: 0.66 to 0.81), while studies with a cut-off level ≥410 ng/mL (0.76, 95% CI: 0.72 to 0.81) had a significantly higher specificity than studies with a cut-off level <410 ng/mL (0.42, 95% CI: 0.38 to 0.47). Therefore the cut-off value may be the source of heterogeneity in both sensitivity and specificity of SII. Similarly, we found that sample size may be the source of sensitivity for mGPS (p<0.001), PLR (p=0.02), GPS (p=0.03), CAR (p=0.04) and LMR (p=0.04), and the source of heterogeneity in the specificity of NLR (p=0.03) and GPS (p<0.001). Additionally, the study area may be the source of heterogeneity in the specificity of mGPS (p=0.01). Also, age and clinical stage may be the source of heterogeneity in specificity for PLR (p<0.001) and PNI (p=0.01), respectively. However, we failed to find the source of heterogeneity for the sensitivity of NLR or PNI and the specificity of CAR or LMR.

Comparison of AUC

Figure 5 shows the summarised receiver-operating characteristic curves of eight indicators. We found that the scope of pooled AUC of CAR (0.72, 95% CI: 0.68 to 0.75) and mGPS (0.75, 95% CI: 0.71 to 0.78) surpassed other indicators except GPS (0.67, 95% CI: 0.63 to 0.71). We further compared CAR, mGPS and GPS by *z* test. The pooled AUC of CAR or mGPS was larger than GPS (p=0.033; p=0.002), but there was no significant difference between CAR and mGPS (online additional file 6).

Publication bias and sensitivity analysis

Only PNI (p=0.03) and mGPS (p=0.02) had a significant publication bias (online additional file 7). The sensitivity analysis of combined DOR showed a robust finding (online additional file 4 and figure 2).

DISCUSSION

In this meta-analysis, we summarised data from 72 studies and estimated the predictive ability of inflammation and nutrition-based indicators in oesophageal cancer. In general, these indicators showed an excellent ability to predict the OS, DFS and CSS of patients with oesophageal cancer. The pretreatment level of CAR and mGPS showed an outstanding prediction value for 5-year OS than other indicators.

Inflammation plays an essential role in the development and progression of various malignant tumours.[14] In addition, nutritional status is closely related to carcinogenesis, cancer growth, tumour progression and tumour prognosis.[15] The peripheral blood cell analysis is a good choice for establishing a prognostic prediction model based on inflammatory and nutrition-related indicators due to its convenience, repeatability and low cost.[16] Previous studies have systematically reviewed the role of some inflammation and nutrition-based indicators in the prognosis of oesophageal cancer, most of which focused on ESCC. Yang *et al*[17] investigated the relationship between NLR and oesophageal cancer by summarising six studies involving 1633 patients. Sun and Zhang[5] reviewed 26 studies to explore the NLR, PLR and LMR in the OS, CSS and DFS in ESCC. Li *et al*[18] reviewed nine observational studies and showed that a low PNI score was significantly correlated with a poor OS of oesophageal cancer and recurrence-free survival of ESCC. Liu *et al* collected eight observational studies and showed that high CAR was related to a worse OS.[19] Although previous meta-analyses have reported the prognostic value of these indicators, this is the first study to comprehensively estimate the popular inflammatory and nutrition-related markers in OS, DFS and CSS of oesophageal cancer. Moreover, this is the first systematic review to summarise the sensitivity and specificity and compare the AUC of these predictors in the 5-year OS of oesophageal cancer.

In this review, we observed that the AUC of CAR and mGPS was significantly higher than NLR, PLR, SII, PNI, LMR and GPS, indicating their outstanding predictive value in oesophageal cancer. CAR and mGPS are calculated based on the level of CRP and albumin. CRP is a kind of acute reactive protein synthesised by liver cells or cancer cells, which can produce an attractive environment for tumour growth, induce DNA damage, promote angiogenesis and favour neoplastic spread and metastasis, revealing levels of inflammation in the body.[20 21] Albumin reflects the malnutrition status of the host, triggers malignant transformation and tumour progression or even causes cachexia.[22] Combining the two indicators can reveal a patient's inflammatory status and nutritional status, which can effectively predict prognosis. These may explain the prominent prognostic role of CAR and mGPS. Additionally, some prospective studies have revealed the better predictive power of CAR and mGPS in other types of cancer. For example, it was reported that the CAR had a better predictive performance for hepatocellular carcinoma and colorectal cancer than NLR, PLR or CRP alone.[23] Other studies demonstrated that mGPS was an independent marker of poor prognosis for patients with SCC and superior to NLR, PLR and PNI.[9]

Although the TNM staging system is well known as a predictive clinical parameter in terms of guiding treatment and clinical prognosis, the survival outcomes for patients with oesophageal cancer with the same TNM

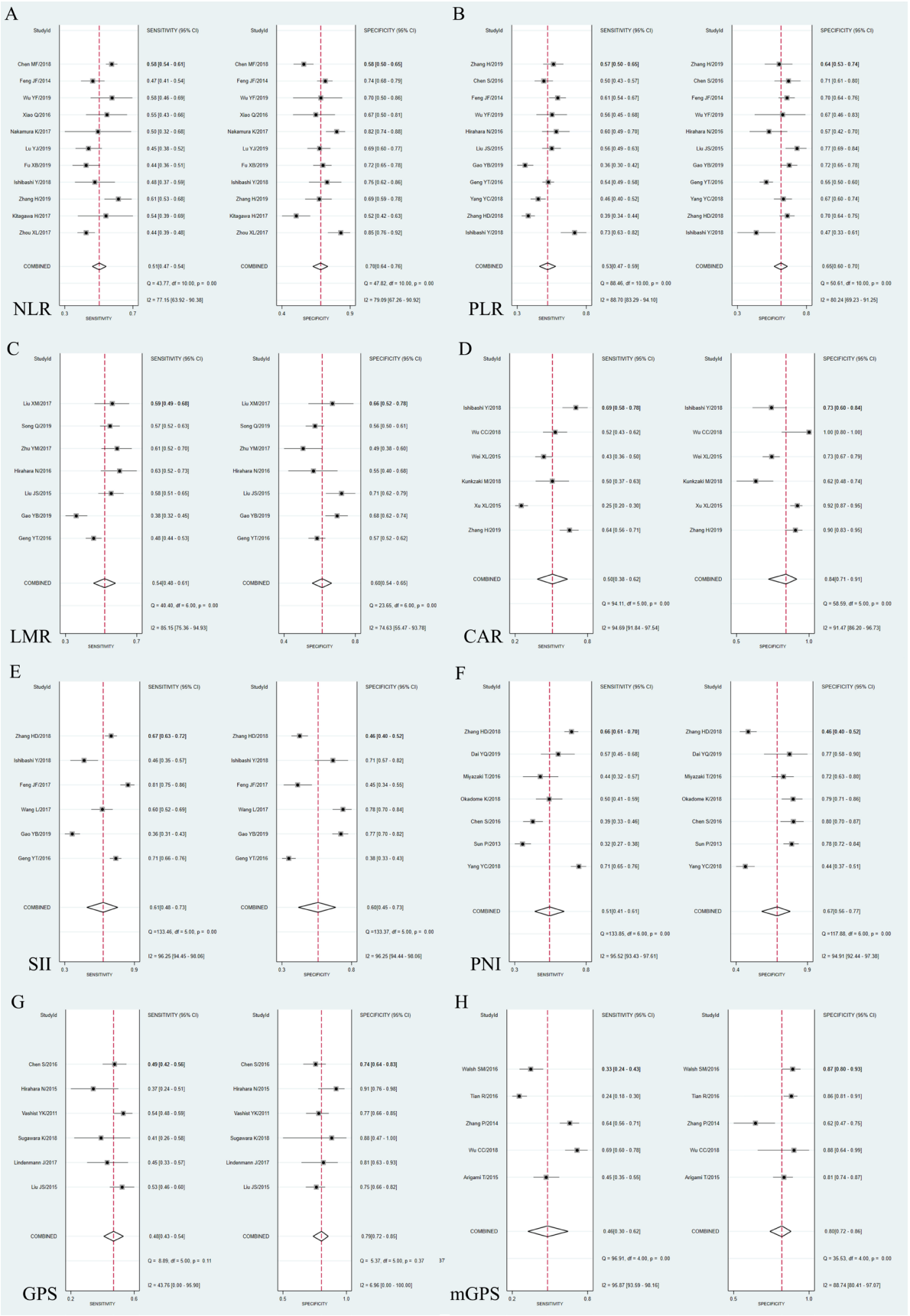

Figure 4 Forest plot of sensitivity and specificity. (A) NLR; (B) PLR; (C) LMR; (D) CAR; (E) SII; (F) PNI; (G) GPS; (H) mGPS. CAR, C reactive protein-to-albumin ratio; GPS, Glasgow Prognostic Score; LMR, lymphocyte-to-monocyte ratio; mGPS, modified Glasgow Prognostic Score; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; Q, Cochran Q statistic; PNI, prognostic nutritional index; SII, systemic inflammation index.

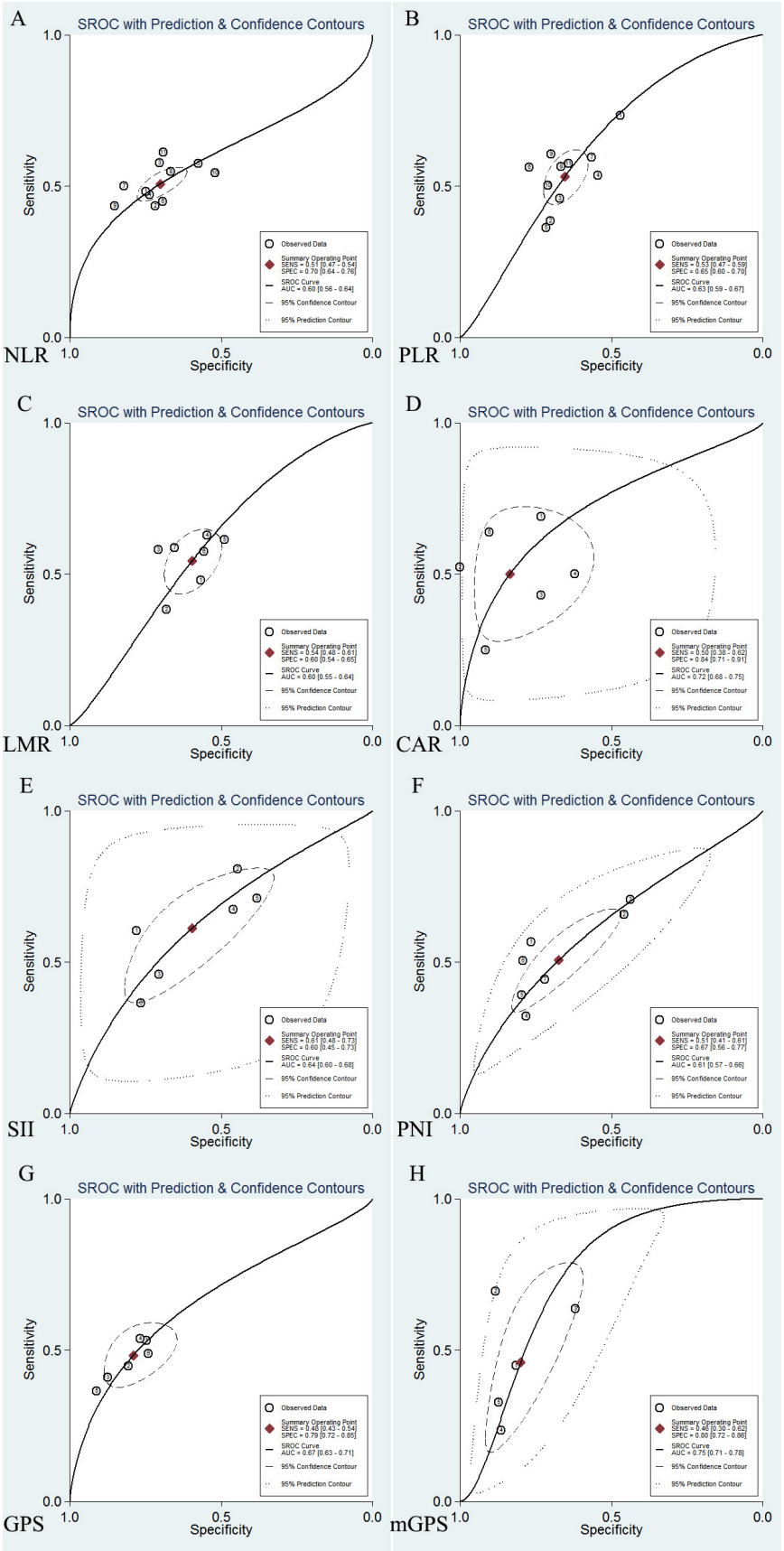

Figure 5 SROC curves of 5-year overall survival. (A) NLR; (B) PLR; (C) LMR; (D) CAR; (E) SII; (F) PNI; (G) GPS; (H) mGPS; AUC, area under curve. CAR, C reactive protein-to-albumin ratio; GPS, Glasgow Prognostic Score; LMR, lymphocyte-to-monocyte ratio; mGPS, modified Glasgow Prognostic Score; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; PNI, prognostic nutritional index; SII, systemic inflammation index. SROC, summary receiver-operating characteristic.

stage still vary widely.[4] In addition, many patients with oesophageal cancer cannot undergo surgery to obtain pathological identification for various reasons. Thus their prognosis cannot be obtained. Moreover, multiple factors influence the prognosis of patients with oesophageal cancer, such as neoadjuvant therapy, psychological factors and behaviour and eating habits, which will change the postoperative pathological stage of the tumour and thus affect the evaluation of disease progression.[24–26] Therefore, pathological diagnosis is not sufficient to accurately predict the prognosis of patients with oesophageal cancer. More readily available objective indicators with high specificity and sensitivity are needed to predict the prognosis of patients with cancer. Our results of this meta-analysis will help clinicians and patients to select appropriate indicators for prognosis prediction. In this way, patients can be classified, and appropriate treatment strategies and postoperative management methods can be selected, providing policymakers with ideas. Taken mGPS as an example, patients with oesophageal cancer with a score of 2 may have a high risk of prognosis, which may provide an effective way for clinicians to select high-risk patients with worse prognosis or severe adverse events before treatment and further timely adjust individualised treatment regimens and enhance postoperative rehabilitation. In addition, policymakers should develop policies to strengthen community guidance and management of such high-risk postoperative patients.

Malnutrition is closely related to carcinogenesis, cancer growth, tumour progression and tumour prognosis.[27] The Global Leadership Initiative on Malnutrition (GLIM) standards integrate current best evidence and expert opinion on malnutrition to promote the prevention, identification and treatment of malnutrition in patients with cancer.[28] Inflammation is one of the aetiological criteria in GLIM classification, and studies have demonstrated that the changes of GPS score, CRP and albumin are highly consistent with the GLIM criteria in identifying malnutrition in patients.[29] Similar to this study, our findings confirm the value of mGPS and CAR in predicting the prognosis of oesophageal cancer. GLIM criteria are re-evaluated every 3–5 years based on new research. Our results may provide a basis for the optimisation of GLIM criteria. Additionally, previous studies have reported that the combination of PNI and GLIM criteria has significant advantages in predicting the incidence and survival rate of perioperative malnutrition.[30] Our results show that the prognostic indicators we studied have high specificity but unsatisfactory sensitivity. More well-designed studies are needed to develop joint indicators to improve the sensitivity and specificity of prediction.

Some limitations should be acknowledged. First, some heterogeneity was not fully explained. This may be due to the fact that some factors that may affect survival were not included, such as living behaviour and eating habits, comorbidities, neoadjuvant therapy and psychological factors.[10 24] Second, the cut-off value of indicators varied between studies, affecting the pooled analysis results and induce unavoidable potential heterogeneity and bias. Therefore, a standard and uniform cut-off value need to be defined. Third, publication bias was detected in studies on PNI and mGPS. Papers that failed to get published due to negative or null results could not be identified in our literature search and thus were not included in the meta-analysis. This may overestimate the prognostic effect of PNI and mGPS. Therefore, more well-designed prospective studies with large samples are needed to verify our findings.

CONCLUSION

NLR, PLR, LMR, PNI, SII, CAR, GPS and mGPS are commonly used as clinical indicators to predict OS, DFS and CSS of oesophageal cancer, but with unsatisfactory sensitivity. Pretreatment CAR and mGPS showed outstanding prognostic values in 5-year OS for patients with oesophageal cancer. Future extensive prospective studies with rigorously designed methodologies are warranted to confirm our results.

Contributors YJ and DX were mainly responsible for data collection, data analysis, drafting and revision. JW participated in the topic design, work plan and paper revision. HS and BQ helped complete the data collection. DT, YJ and ZL involved in the data analysis and paper revision. YJ, DX and HS contributed equally to this paper. All authors finally approved the version to be published and agreed to be accountable for all aspects of the work.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval All data were downloaded from the public database and followed the data access policies. This study was exempted from ethical review by the ethics committee of Nanjing Medical University. This study did not involve individual information, so there was no requirement for informed consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. All data generated or analyzed during this study are included in this published article.

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REFERENCES

1 Arnold M, Abnet CC, Neale RE, *et al*. Global burden of 5 major types of gastrointestinal cancer. *Gastroenterology* 2020;159:335–49.
2 Sung H, Ferlay J, Siegel RL, *et al*. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209–49.
3 Huang F-L, Yu S-J. Esophageal cancer: risk factors, genetic association, and treatment. *Asian J Surg* 2018;41:210–5.
4 Gong YB, Zhu Z, Wang X, *et al*. [Influence of different biological behaviors on prognosis of patients with advanced gastric cancer at the same TNM stage]. *Zhonghua Wei Chang Wai Ke Za Zhi* 2020;23:953–62.
5 Sun Y, Zhang L. The clinical use of pretreatment NLR, PLR, and LMR in patients with esophageal squamous cell carcinoma: evidence from a meta-analysis. *Cancer Manag Res* 2018;10:6167–79.
6 Zhang H, Shang X, Ren P, *et al*. The predictive value of a preoperative systemic immune-inflammation index and prognostic nutritional index in patients with esophageal squamous cell carcinoma. *J Cell Physiol* 2019;234:1794–802.
7 Fu X, Li T, Dai Y, *et al*. Preoperative systemic inflammation score (SIS) is superior to neutrophil to lymphocyte ratio (NLR) as a predicting indicator in patients with esophageal squamous cell carcinoma. *BMC Cancer* 2019;19:721.
8 Okadome K, Baba Y, Yagi T, *et al*. Prognostic nutritional index, tumor-infiltrating lymphocytes, and prognosis in patients with esophageal cancer. *Ann Surg* 2020;271:693–700.
9 Fan H, Shao Z-Y, Xiao Y-Y, *et al*. Comparison of the glasgow prognostic score (GPs) and the modified glasgow prognostic score (mGPS) in evaluating the prognosis of patients with operable and inoperable non-small cell lung cancer. *J Cancer Res Clin Oncol* 2016;142:1285–97.
10 Akgun E, Ozkok S, Tekin M, *et al*. The effects of chemoradiotherapy on recurrence and survival in locally advanced rectal cancers with curative total mesorectal excision: a prospective, nonrandomized study. *World J Surg Oncol* 2017;15:205.
11 Whiting PF, Rutjes AWS, Westwood ME, *et al*. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011;155:529–36.
12 Zamora J, Abraira V, Muriel A, *et al*. Meta-disc: a software for meta-analysis of test accuracy data. *BMC Med Res Methodol* 2006;6:31.
13 Moses LE, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. *Stat Med* 1993;12:1293–316.
14 Ostan R, Lanzarini C, Pini E, *et al*. Inflammaging and cancer: a challenge for the mediterranean diet. *Nutrients* 2015;7:2589–621.
15 Steenhagen E, van Vulpen JK, van Hillegersberg R, *et al*. Nutrition in peri-operative esophageal cancer management. *Expert Rev Gastroenterol Hepatol* 2017;11:663–72.
16 Wu Y, Ye S, Goswami S, *et al*. Clinical significance of peripheral blood and tumor tissue lymphocyte subsets in cervical cancer patients. *BMC Cancer* 2020;20:173.
17 Yang Y, Xu H, Zhou L, *et al*. Platelet to lymphocyte ratio is a predictive marker of prognosis and therapeutic effect of postoperative chemotherapy in non-metastatic esophageal squamous cell carcinoma. *Clin Chim Acta* 2018;479:160–5.
18 Li P, Wang X, Lai Y, *et al*. The prognostic value of pre-treatment prognostic nutritional index in esophageal squamous cell carcinoma: a meta-analysis. *Medicine* 2019;98:e15280.
19 Liu Z, Shi H, Chen L. Prognostic role of pre-treatment C-reactive protein/albumin ratio in esophageal cancer: a meta-analysis. *BMC Cancer* 2019;19:1161.
20 Aiolfi A, Asti E, Rausa E, *et al*. Use of C-reactive protein for the early prediction of anastomotic leak after esophagectomy: systematic review and Bayesian meta-analysis. *PLoS One* 2018;13:e0209272.
21 Morris-Stiff G, Gomez D, Prasad KR. C-reactive protein in liver cancer surgery. *Eur J Surg Oncol* 2008;34:727–9.
22 Mantzorou M, Koutelidakis A, Theocharis S, *et al*. Clinical value of nutritional status in cancer: what is its impact and how it affects disease progression and prognosis? *Nutr Cancer* 2017;69:1151–76.
23 Ni X-C, Yi Y, Fu Y-P, *et al*. Prognostic value of the modified Glasgow prognostic score in patients undergoing radical surgery for hepatocellular carcinoma. *Medicine* 2015;94:e1486.
24 Taira N, Iwata H, Hasegawa Y, *et al*. Health-related quality of life and psychological distress during neoadjuvant endocrine therapy with letrozole to determine endocrine responsiveness in postmenopausal breast cancer. *Breast Cancer Res Treat* 2014;145:155–64.
25 Pierce JP, Natarajan L, Caan BJ, *et al*. Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: the women's healthy eating and living (WHEL) randomized trial. *JAMA* 2007;298:289–98.
26 Ohashi S, Miyamoto Shin'ichi, Kikuchi O, *et al*. Recent advances from basic and clinical studies of esophageal squamous cell carcinoma. *Gastroenterology* 2015;149:1700–15.
27 Marian M, August DA. Prevalence of malnutrition and current use of nutrition support in cancer patient study. *JPEN J Parenter Enteral Nutr* 2014;38:163–5.
28 Jensen GL, Cederholm T, Correia MITD, *et al*. GLIM criteria for the diagnosis of malnutrition: a consensus report from the global clinical nutrition community. *JPEN J Parenter Enteral Nutr* 2019;43:32–40.
29 Contreras-Bolívar V, Sánchez-Torralvo FJ, Ruiz-Vico M, *et al*. GLIM criteria using hand grip strength adequately predict six-month mortality in cancer inpatients. *Nutrients* 2019;11:2043.
30 Wang P, Chen X, Liu Q, *et al*. Good performance of the global leadership initiative on malnutrition criteria for diagnosing and classifying malnutrition in people with esophageal cancer undergoing esophagectomy. *Nutrition* 2021;91-92:111420–2.

Searching strategy:

((((((((((NLR OR neutrophil to lymphocyte ratio) OR neutrophil-to-lymphocyte ratio) OR neutrophillymphocyte ratio) OR neutrophil lymphocyte ratio) OR (((((PLR OR platelet lymphocyte ratio) OR plateletlymphocyte ratio) OR platelet to lymphocyte ratio) OR platelet-to-lymphocyte ratio) OR platelet lymphocyte ratio)) OR (((((LMR OR lymphocyte monocyte ratio) OR lymphocytemonocyte ratio) OR lymphocyte to monocyte ratio) OR lymphocyte-to-monocyte ratio) OR lymphocyte monocyte ratio)) OR ((((SII OR Systemic Immune-Inflammation Index) OR Systemic Immune Inflammation Index) OR Systemic Inflammation Index) OR Systemic Immune-Inflammation Indices)) OR (PNI OR Prognostic nutritional index)) OR (((GPS OR Glasgow Outcome Scale) OR GOS) OR Glasgow Prognostic score)) OR (mGPS OR modified Glasgow Prognostic score)) AND ((((ESCC OR esophageal neoplasm) OR esophageal cancer) OR esophageal carcinoma) OR esophageal squamous cell carcinoma))

Table 1. The characteristics of the studies included.

Study	Ethnicity (country)	Sample size	Gender (M/F)	Age	Stage	NLR cutoff	PLR cutoff	LMR cutoff	PNI cutoff	SII cutoff	GPS cutoff	mGPS cutoff	CAR cutoff	Follow-up (months)	Treatment	Outcome	pathology	TP /FP /FN /TN (OS)
Wang L et al. (2017)[1]	China	280	233/47	64.071±7.412	0-IV	2	159	5.3	NR	560	NR	NR	NR	36	surgery	OS/DFS	SCC	SII:81 32 53 114
Feng JF et al. (2017)[2]	China	298	260/38	NR	I-III	5	150	NR	NR	410	NR	NR	NR	NR	surgery	CSS	SCC	SII:165 52 39 42
Nakatani M et al. (2017)[3]	Japan	66	56/10	64.7 ± 6.1	II-III	NR	NR	NR	45	NR	NR	NR	NR	31.9	surgery	OS/RFS	SCC	NR
Kubo N et al. (2017)[4]	Japan	202	162/40	63.73 ± 7.93	I-IV	NR	NR	NR	44	NR	NR	NR	NR	47.1	surgery	OS/RFS	SCC	NR
Hirahara N et al. (2018)[5]	Japan	169	150/19	PNI＜49.2：67.1±8.2 PNI≥49.2：65.4±8.0	Ia-IIIc	NR	NR	NR	49.2	NR	NR	NR	NR	NR	surgery	OS/CSS	SCC	NR
Dai YQ et al. (2019)[6]	China	106	79/27	<65:82; ≥65:24	T1-4/N0-1	2.1	104.1	3.45	48.15	305.6	NR	NR	NR	19(2–190)	CRT	OS	SCC	PNI: 43 7 33 23
Ishibashi Y et al. (2018)[7]	Japan	143	121/22	70.6 ± 8.4(43–90)	I-IV	3	135	NR	NR	650	NR	NR	0.085	NR	surgery	OS/CSS	SCC/ADC /Others	SII: 39 17 46 41 NLR: 42 14 45 42 PLR: 66 28 24 25 CAR: 60 15 27 41
Zhang HD et al. (2018)[8]	China	655	537/118	61(27–88)	0-III	1.87	140.09	NR	52.28	387.65	NR	NR	NR	36.0(3–144)	surgery	OS	SCC	PLR: 148 81 236 190 SII: 259 146 125 125 PNI: 264 137 138 116
Yang YC et al. (2018)[9]	China	515	418/97	61(33–92)	I-III	1.2	130	NR	57	NR	NR	NR	NR	35(2–106)	surgery	OS	SCC	PLR: 143 67 168 137 PNI: 217 117 90 91
Wu CC et al. (2018)[10]	China	126	122/4	58(37–80)	IIIa-IIIc	2.5	103	NR	NR	NR	NR	0/1,2	0.95	NR	mixed	OS	SCC	CAR: 57 1 52 17 mGPS: 77 2 34 15
Wei XL et al. (2015)[11]	China	423	341/82	58(24–88)	I-IV	1.835	163.8	NR	49.05	NR	NR	0,1,2	0.095	35.7(0.6–95.6)	surgery	OS	SCC	CAR: 90 57 119 157
Geng YT et al. (2016)[12]	China	916	696/220	60.0(37–84)	0-III	1.7	120	3.57	NR	307	NR	NR	NR	39(3–146)	surgery	OS	SCC	SII: 279 227 113 140 LMR: 239 181

																	258 238 PLR: 275 183 238 220
Gao YB et al. (2019)[13]	China	468	376/92	59.5(36–81)	I-III	2.27	117.05	5.26	NR	479.72	NR	NR	NR	49.1±32.6(3.2–114.5)	surgery	OS/DFS	SCC	SII: 93 50 162 163 PLR: 93 60 164 151 LMR: 96 69 155 148
Liu JS et al. (2015)[14]	China	326	283/43	59.2±7.9(38-80)	T1-4/N0-3	3.45	166	2.3	NR	NR	0/1,2	NR	NR	45	surgery	CSS	SCC	GPS: 108 31 95 92 PLR: 114 28 89 95 LMR: 112 36 81 87
Hirahara N et al. (2016)[15]	Japan	147	132/15	<70：46 ≥70：101	Ia-IIIc	1.6	147	4	NR	NR	NR	NR	NR	42(3-111)	surgery	OS/CSS	SCC	LMR: 59 24 35 29 PLR: 56 23 38 30
Han LH et al. (2015)[16]	China	218	177/41	60.5(32-84)	I-III	2.6	244	2.57	NR	NR	NR	NR	NR	38.6(3-71)	surgery	OS/DFS	SCC	NR
Gao QF et al. (2018)[17]	China	153	128/25	61.93±6.72	0-III	2.1	145.9	2.3	NR	NR	NR	NR	NR	NR	surgery	OS	SCC	NR
Kunkzaki M et al. (2018)[18]	Japan	116	98/18	66(44-83)	0-IV	5	150	NR	45	NR	0/1,2	0/1,2	0.042	NR	mixed	OS	SCC	CAR: 29 22 29 36
Xu XL et al. (2015)[19]	China	468	416/52	58	I-IIIc	2.4	147	NR	NR	NR	0/1/2	0/1/2	0.5	49.9(10.9–88.0)	surgery	OS	NR	CAR: 72 15 216 165
Toyokawa T et al. (2016)[20]	Japan	185	152/33	64(59–70)	I-IV	3.612	193	NR	NR	NR	0/1,2	NR	NR	81.5(IQR:45.8–112.3)	surgery	OS/RFS	SCC	NR
Li KJ et al. (2019)[21]	China	204	171/33	65.8(38-85)	T1-4/N0-2	2.64	NR	3.03	NR	NR	NR	NR	NR	11.5(2.1-77.4)	CRT	OS/RFS	SCC	NR
Fu XB et al. (2019)[22]	China	357	279/78	57(34-77)	I-IVa	2.27	NR	2.57	NR	SIS:0/1/2	NR	NR	NR	58(1–84)	surgery	OS	SCC	NLR: 77 50 100 128
Zhang F et al. (2016)[23]	China	468	376/92	60(36-81)	I-III	2.5	117.07	NR	NR	NR	NR	NR	NR	49.1±32.6(3.2-114.5)	surgery	OS/DFS	SCC	NR
Xie X et al. (2016)[24]	China	317	244/73	58.1±8.9(34–76)	I-III	2.1	103	NR	NR	NR	NR	NR	NR	46(36–62)	surgery	DSS	SCC	NR
Wu YF et al. (2019)[25]	China	105	98/7	57.69±8.6(38-81)	I-III	4.35	NR	NR	NR	NR	NR	NR	NR	19.5±14.1	CRT	OS/PFS	SCC	PLR: 44 9 34 18 NLR: 45 8 33 19
Feng JF et	China	483	411/72	59.1±8.0(34-80)	T1-4/N-+	3.5	150	NR	NR	NR	NR	NR	NR	NR	surgery	OS	SCC	NLR:115 63 129

al. (2014)[26]																	176 PLR: 148 72 96 167
Zhu YM et al. (2017)[27]	China	220	117/103	≤60/>60:124/96	T3N0M0	NR	NR	3.364	NR	NR	NR	NR	NR	DFS:40.0(34.2–45.8) OS:53.0(48.0–58.0)	mixed	OS/DFS	SCC	LMR: 81 45 51 43
Song Q et al. (2019)[28]	China	680	582/98	61(56-67)	Ia-IIIc	NR	NR	3.17	NR	NR	NR	NR	NR	NR	mixed	OS/DFS	SCC	LMR: 182 161 135 202
Chen MF et al. (2018)[29]	China	1168	1113/55	(<50/50-64/>64): 344/609/215	≤T2/T3-T4,N0/N+	3	NR	NR	NR	NR	NR	NR	NR	NR	mixed	OS/DFS	SCC	NLR: 567 77 419 105
Duan H et al. (2015)[30]	China	371	276/95	57.7±8.9	Ib-IIIc	3	NR	NR	NR	410	NR	NR	NR	66(49-76)	surgery	CSS/RFS	SCC	NR
Gao GD et al. (2017)[31]	China	1281	988/293	Survival/Dead(634/647) 57.7±8.9/60.2±27.7	0-IV	2.86	NR	NR	NR	NR	NR	NR	NR	NR	mixed	OS	SCC	NR
Han FY et al. (2019)[32]	China	354	267/87	<60/>=60:100/254	I-IV	1.88	NR	NR	NR	NR	NR	NR	NR	26(2-80)	surgery	OS/DFS	SCC/ADC /Others	NR
Hirahara Noriyuki et al. (2018)[33]	Japan	148	132/16	CONUT 0/1/2-3(48/37/11) 61.5±5.4/61.8±5.9/60.4±5.3	Ia-IIIc	3.5	NR	NR	NR	NR	NR	NR	NR	NR	surgery	CSS	SCC	NR
Kosumi K et al. (2016)[34]	Japan	313	248/35	<65/≥65(118/165)	0-IV	1.94	NR	NR	NR	NR	NR	NR	NR	33.6	surgery	OS/CSS	SCC	NR
Lu YJ et al. (2019)[35]	China	315	259/56	59(35-75)	I-IVa	3.18	NR	NR	NR	NR	NR	NR	NR	NR	surgery	OS	SCC	NLR: 87 37 107 84
Nakamura K et al. (2017)[36]	Japan	245	219/26	<65/≥65:110/135	T1a-b/N0-3	2.42	NR	NR	NR	NR	NR	NR	NR	37.2	surgery	OS/DFS	SCC/ADC /Others	NLR: 16 22 16 101
Sharaiha RZ et al. (2011)[37]	USA	295	237/58	62.8	I-IV	5	NR	NR	NR	NR	NR	NR	NR	31(13–61)	surgery	OS/DFS	SCC/ADC /Others	NR
Xiao Q et al. (2016)[38]	China	121	106/15	62(30–76)	I-III	1.77	NR	NR	NR	NR	NR	NR	NR	28.0(1–102)	surgery	OS/RFS	SCC	NLR: 45 13 37 26
Zhou XL et al. (2017)[39]	China	517	407/110	65(36–74)	II-IV	5	NR	NR	NR	NR	NR	NR	NR	17(2-76)	CRT	OS/PFS	SCC	NLR: 188 12 244 69
Arigami T et al. (2015)[40]	Japan	238	210/28	65(37–87)	I-III	3	NR	NR	NR	NR	NR	0/1,2	NR	26(1-182)	surgery	OS	SCC	mGPS: 44 26 54 114
Lindenmann J et al. (2017)[41]	Austria	174	148/26	61.1(22-81)	T0-4/N0-3	NR	NR	NR	NR	NR	1-2 vs 0	NR	NR	NR	mixed	AC/CSS	ADC/SCC	GPS: 33 6 41 25
Ma QL et	China	725	539/186	58(32-80)	TNM I/II/III	NR	NR	NR	NR	NR	1-2 vs	NR	NR	28	surgery	CSS	SCC	NR

al. (2016)[42]											0						
Okuno T et al. (2017)[43]	Japan	142	119/12	62(37–75)	(UICC 5th) IIB/III/IVa/IVb	NR	NR	NR	NR	NR	1 vs 0 2 vs 0	NR	NR	NR	CRT	OS	SCC	NR
Sugawara K et al. (2018)[44]	Japan	47	32/15	63(47–81)	I/II/III/Iva/IVb	NR	NR	NR	NR	NR	1 vs 0 2 vs 0	NR	NR	26.5(4.4–97.9)	surgery	OS	SCC/ADC	GPS: 16 1 23 7
Vashist YK et al. (2011)[45]	Germany	495	391/104	63.2(34.5–85.2)	T1-4/N-+/M-+	NR	NR	NR	NR	NR	0 vs 1	NR	NR	NR	surgery	OS/CSS	ADC/SCC	GPS: 188 20 161 66
Hirahara N et al. (2015)[46]	Japan	141	97/12	NR	Ia-IIIc	2.5	NR	NR	NR	NR	1-2 vs 0	NR	NR	NR	surgery	OS	NR	GPS: 19 3 33 31
Kitagawa H et al. (2017)[47]	Japan	140	112/28	65(43–85)	I-IV	NR	NR	NR	NR	NR	1-2 vs 0	NR	NR	36.6	mixed	OS/DFS	SCC/ADC /others	NLR: 25 45 21 49
Jomrich G et al. (2017)[48]	Austria	449	225/58	63(31–88)	UICC stage:0-4	NR	NR	NR	NR	NR	1 vs 0 2 vs 0	1 vs 0 2 vs 0	0.95	63(35-95)	surgery	OS/DFS	SCC/ADC	NR
Kimura J et al. (2016)[49]	Japan	142	131/11	65.1(40–82)	III and IV	NR	NR	NR	NR	NR	1 vs 0 2 vs 0	1 vs 0 2 vs 0	NR	NR	CT+RT	PFS/DFS/ CSS	SCC	NR
Chen P et al. (2017)[50]	China	163	134/29	57(31–79)	II/IV	NR	NR	NR	NR	NR	NR	0 vs 1 0 vs 2	NR	NR	radiotherapy	OS	SCC	NR
Otowa Y et al. (2016)[51]	Japan	100	88/12	68(44–82)	II/III	NR	NR	NR	NR	NR	NR	Pre-NAC 0 vs 1/2 Post-NAC 0 vs 1	NR	20.8(4.6–79.5)	surgery	OS	SCC	NR
Tian R et al. (2016)[52]	China	442	331/111	60.0(20.0-88.0)	I/II/III	NR	NR	NR	NR	NR	NR	1-2 vs 0	NR	DFS:35.6(24.3-46.9) OS:57.4(37.8-77.0)	surgery	OS/PFS	SCC	mGPS: 52 30 169 191
Walsh SM et al. (2016)[53]	Ireland	223	187/36	64(30–87)	I/II/III	NR	NR	NR	NR	NR	NR	1-2 vs 0	NR	21	surgery	OS/RFS	ADC	mGPS: 34 15 70 104
Zhang P et al. (2014)[54]	China	212	166/46	60.0(37-81)	I-II/ III/IV	NR	NR	NR	NR	NR	NR	0 vs 1 vs 2	NR	35.0(2-72)	radiotherapy	OS/PFS	SCC	mGPS: 103 19 59 31
Sun P et al. (2013)[55]	China	502	382/120	58.23±9.33	I–IV	NR	NR	NR	50	NR	NR	NR	NR	30	NR	OS	SCC	PNI: 92 47 194 169
Chen S al. (2016)[56]	China	308	268/40	NR	I–III	3.5	150	NR	45	NR	GPS1 vs GPS0, GPS2 vs	NR	NR	NR	Surgery		SCC	PNI: 83 19 129 74 GPS: 105 24 110 69 PLR:: 108 27

											GPS0						107 66
Okadome K et al. (2018)[57]	Japan	337	300/37	65.9	I–IV	NR	NR	NR	45	NR	NR	NR	NR	60	Surgery	OS/CSS	SCC/ADC /Others	PNI: 63 24 62 92
Migita K et al. (2018)[58]	Japan	137	76/16	NR	T1-T4/N0-N+	2.2	NR	NR	47	NR	NR	NR	NR	NR	mixed	OS	SCC	NR
Zhang H et al. (2019)[59]	China	266	172/94	67(48-87)	I–III	3.06	145.26	NR	NR	NR	NR	NR	0.13	NR	curative RT only or concurrent CRT	OS	SCC	NLR: 107 28 68 63 PLR: 100 33 74 59 CAR: 104 10 59 93
Otowa Y et al. (2017)[60]	Japan	149	129/20	66.9±8.3	II/III	NR	NR	NR	NR	NR	NR	NR	0.030	NR	Mixed	OS	SCC	NR
Liu XQ et al. (2019)[61]													0.15		radical radiotherapy	OS		NR
Shao YJ et al. (2015)[62]	China	916 primary:633 validation:283	primary :484/149 validation:211/72	Primary:60(37–83) Validation:61(38–84)	I–III	1.7	120	3.57	NR	NR	0/1/2	0/1/2	0.06/0.12	39(3-146.2)	Surgery	OS	SCC	NR
Liu DQ et al. (2016)[63]	China	260	217/43	59(39–83)	I-IV	NR	NR	NR	NR	NR	0/1/2	NR	NR	40.5 (2–91)	surgery	OS/DFS	SCC	NR
Wang CY et al. (2012)[64]	Taiwan, China	271	261/10	NR	I-IV	NR	NR	NR	NR	NR	0/1,2	NR	NR	30 (5–81)	mixed	OS	SCC/ADC	NR
Feng JF et al. (2014)[65]	China	493	420/73	59.1(34 to 80)	T1-4a/N-+	NR	NR	NR	NR	NR	2/0	NR	NR	45	surgery	NR	SCC	NR
Lindenmann J et al. (2014)[66]	Austria	214	181/33	67 ± 11.84(21–93)	III-IV	NR	NR	NR	NR	NR	0/1/2	NR	NR	NR	CT+RT	NR	SCC/ADC	NR
Matsuda S et al. (2015)[67]	Japan	199	180/19	62.9 ± 8.29	I-IV	NR	NR	NR	NR	NR	0/1/2	NR	NR	28.5	mixed	OS/DFS	SCC/ADC /Others	NR
Liu XM et al. (2017)[68]	China	162	127/35	63 (38–70)	II-III	NR	NR	4.02	NR	NR	NR	NR	NR	23.3 (8–43.7)	mixed	OS/PFS	SCC	LMR: 61 20 43 38
Tian R et al. (2016)[69]	China	260	193/67	59.0 (20.0-87.0)	I-III	NR	NR	NR	NR	NR	NR	0/1,2	NR	46.5	surgery	OS/DFS	SCC	NR
Nakamura M et al. (2014)[70]	Japan	168	135/33	67(47–85)	0-IV	NR	NR	NR	NR	NR	NR	0 vs 2	NR	39(5–99)	mixed	NR	SCC	NR
Han LH et al. (2015)[71]	China	206	165/41	60(32-84)	I-IV/T1-4/N0-3	NR	NR	2.9	45.5	NR	NR	NR	NR	39.5(3-71)	surgery	OS/DFS	SCC	NR
Miyazaki T et al.	Japan	192	173/19	65.8(42-86)	I-IV/T1-4/N0-3/M0-1	3.49	NR	NR	47.7	NR	NR	NR	NR	26.5(1-108)	surgery	OS	NR	PNI: 31 34 39 88

(2016)[72]	

Abbreviations: OS, overall survival; CSS, cancer-specific survival; DFS, disease-free survival; EC, esophageal carcinoma; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; CAR, c-reactive protein-to-albumin ratio; SII, systemic inflammation index; PNI, prognostic nutritional index; GPS, Glasgow Prognostic Score; mGPS, modified Glasgow Prognostic Score; TP, true-positive; FP, false-positive; TN, true-negative; FN, false-negative

Reference

[1] Wang L, Wang C, Wang JF, Huang XC, Cheng YF. A novel systemic immune-inflammation index predicts survival and quality of life of patients after curative resection for esophageal squamous cell carcinoma. Journal of Cancer Research and Clinical Oncology, 2017, 143(10):2077-2086.

[2] Feng JF, Chen S, Yang X. Systemic immune-inflammation index (SII) is a useful prognostic indicator for patients with squamous cell carcinoma of the esophagus. Medicine, 2017, 96(4).

[3] Nakatani M, Migita K, Matsumoto S, Wakatsuki K, Ito M, Nakade H, Kunishige T, Kitano M, Kanehiro H. Prognostic significance of the prognostic nutritional index in esophageal cancer patients undergoing neoadjuvant chemotherapy. Diseases of the Esophagus, 2017, 30(8).

[4] Kubo N, Ohira M, Tamura T, Sakurai K, Toyokawa T, Tanaka H, Yashiro M, Yamashita Y, Hirakawa K. Prognostic significance of baseline nutritional index for patients with esophageal squamous cell carcinoma after radical esophagectomy. Esophagus, 2017, 14(1):84-90.

[5] Hirahara N, Tajima Y, Fujii Y, Kaji S, Yamamoto T, Hyakudomi R, Taniura T, Miyazaki Y, Kishi T, Kawabata Y. Preoperative Prognostic Nutritional Index Predicts Long-Term Surgical Outcomes in Patients with Esophageal Squamous Cell Carcinoma. World Journal of Surgery, 2018, 42(7):2199-2208.

[6] Dai YQ, Fu XB, Li TT, Yao QW, Su LY, Su HY, Li JC. Long-term impact of prognostic nutritional index in cervical esophageal squamous cell carcinoma patients undergoing definitive radiotherapy. Annals of Translational Medicine, 2019, 7(8).

[7] Ishibashi Y, Tsujimoto H, Hiraki S, Kumano I, Yaguchi Y, Horiguchi H, Nomura S, Ito N, Shinto E, Aosasa S, Yamamoto J, Ueno H. Prognostic Value of Preoperative Systemic Immunoinflammatory Measures in Patients with Esophageal Cancer. Annals of Surgical Oncology, 2018, 25(11):3288-3299.

[8] Zhang HD, Shang XB, Ren P, Gong L, Ahmed A, Ma Z, Ma R, Wu XX, Xiao XM, Jiang HJ, Tang P, Yu ZT. The predictive value of a preoperative systemic immune-inflammation index and prognostic nutritional index in patients with esophageal squamous cell carcinoma. Journal of Cellular Physiology, 2019, 234(2):1794-1802.

[9] Yang YC, Xu H, Zhou LK, Deng T, Ning T, Liu R, Zhang L, Wang X, Ge SH, Li HL, Ba Y. Platelet to lymphocyte ratio is a predictive marker of prognosis and therapeutic effect of postoperative chemotherapy in non-metastatic esophageal squamous cell carcinoma. Clinica Chimica Acta, 2018, 479:160-165.

[10] Wu CC, Li SH, Lu HI, Lo CM, Wang YM, Chou SY, Chen YH. Inflammation-based prognostic scores predict the prognosis of locally advanced cervical esophageal squamous cell carcinoma patients receiving curative concurrent chemoradiotherapy: a propensity score-matched analysis. Peerj, 2018, 6.

[11] Wei XL, Wang FH, Zhang DS, Qiu MZ, Ren C, Jin Y, Zhou YX, Wang DS, He MM, Bai L, Wang F, Luo HY, Li YH, Xu RH. A novel inflammation-based prognostic score in esophageal squamous cell carcinoma: the C-reactive protein/albumin ratio. Bmc Cancer, 2015, 15.

[12] Geng YT, Shao YJ, Zhu DX, Zheng X, Zhou Q, Zhou WJ, Ni XF, Wu CP, Jiang JT. Systemic Immune-Inflammation Index Predicts Prognosis of Patients with Esophageal Squamous Cell Carcinoma: A Propensity Score-matched Analysis. Scientific Reports, 2016, 6.

[13] Gao YB, Guo W, Cai SH, Zhang F, Shao F, Zhang GC, Liu TJ, Tan FW, Li N, Xue Q, Gao SG, He J. Systemic immune-inflammation index (SII) is useful to predict survival outcomes in patients with surgically resected esophageal squamous cell carcinoma. Journal of Cancer, 2019, 10(14):3188-3196.

[14] Liu JS, Huang Y, Yang X, Feng JF. A nomogram to predict prognostic values of various inflammatory biomarkers in patients with esophageal squamous cell carcinoma. American Journal of Cancer Research, 2015, 5(7):2180-2189.

[15] Hirahara N, Matsubara T, Kawahara D, Nakada S, Ishibashi S, Tajima Y. Prognostic significance of preoperative inflammatory response biomarkers in patients undergoing curative thoracoscopic esophagectomy for esophageal squamous cell carcinoma. Ejso, 2016, 43(2):493-501.

[16] Han LH, Jia YB, Song QX, Wang JB, Wang NN, Cheng YF. Prognostic significance of preoperative lymphocyte-monocyte ratio in patients with resectable esophageal squamous cell carcinoma. Asian Pac J Cancer Prev, 2015, 16(6):2245-2250.

[17] Gao QF, Qiu JC, Huang XH, Xu YM, Li SQ, Sun F, Zhang J, Yang WM, Min QH, Jiang YH, Chen QG, Zhang L, Wang XZ, Ying HQ. The predictive and prognostic role of a novel ADS score in esophageal squamous cell carcinoma patients undergoing esophagectomy. Cancer Cell International, 2018, 18.

[18] Kunizaki M, Tominaga T, Wakata K, Miyazaki T, Matsumoto K, Sumida Y, Hidaka S, Yamasaki T, Yasutake T, Sawai T, Hamamoto R, Nanashima A, Nagayasu T. Clinical significance of the C-reactive protein-to-albumin ratio for the prognosis of patients with esophageal squamous cell carcinoma. Mol Clin Oncol, 2018, 8(2):370-374.

[19] Xu XL, Yu HQ, Hu W, Song Q, Mao WM. A Novel Inflammation-Based Prognostic Score, the C-Reactive Protein/Albumin Ratio Predicts the Prognosis of Patients with Operable Esophageal Squamous Cell Carcinoma. Plos One, 2015, 10(9).

[20] Toyokawa T, Kubo N, Tamura T, Sakurai K, Amano R, Tanaka H, Muguruma K, Yashiro M, Hirakawa K, Ohira M. The pretreatment Controlling Nutritional Status (CONUT) score is an independent prognostic factor in patients with resectable thoracic

esophageal squamous cell carcinoma: results from a retrospective study. Bmc Cancer, 2016, 16.

[21] Li KJ, Xia XF, Su M, Zhang H, Chen WH, Zou CL. Predictive value of lymphocyte-to-monocyte ratio (LMR) and neutrophil-to-lymphocyte ratio (NLR) in patients with oesophageal cancer undergoing concurrent chemoradiotherapy. Bmc Cancer, 2019, 19(1).

[22] Fu XB, Li TT, Dai YQ, Li JC. Preoperative systemic inflammation score (SIS) is superior to neutrophil to lymphocyte ratio (NLR) as a predicting indicator in patients with esophageal squamous cell carcinoma. Bmc Cancer, 2019, 19.

[23] Zhang F, Chen ZL, Wang P, Hu XD, Gao YB, He J. Combination of platelet count and mean platelet volume (COP-MPV) predicts postoperative prognosis in both resectable early and advanced stage esophageal squamous cell cancer patients. Tumor Biology, 2016, 37(7):9323-9331.

[24] Xie X, Luo KJ, Hu Y, Wang JY, Chen J. Prognostic value of preoperative platelet-lymphocyte and neutrophil-lymphocyte ratio in patients undergoing surgery for esophageal squamous cell cancer. Diseases of the Esophagus, 2016, 29(1):79-85.

[25] Wu YF, Chu SC, Chang BS, Cheng YT, Wang TF. Hematologic Markers as Prognostic Factors in Nonmetastatic Esophageal Cancer Patients under Concurrent Chemoradiotherapy. Biomed Research International, 2019.

[26] Feng JF, Huang Y, Chen QX. Preoperative platelet lymphocyte ratio (PLR) is superior to neutrophil lymphocyte ratio (NLR) as a predictive factor in patients with esophageal squamous cell carcinoma. World Journal of Surgical Oncology, 2014, 12.

[27] Zhu YM, Li MH, Bo C, Liu XM, Zhang JB, Li ZX, Zhao F, Kong L, Yu JM. Prognostic significance of the lymphocyte-to-monocyte ratio and the tumor-infiltrating lymphocyte to tumor-associated macrophage ratio in patients with stage T3N0M0 esophageal squamous cell carcinoma. Cancer Immunology Immunotherapy, 2017, 66(3):343-354.

[28] Song Q, Wu JZ, Wang S. Low Preoperative Lymphocyte to Monocyte Ratio Serves as a Worse Prognostic Marker in Patients with Esophageal Squamous Cell Carcinoma Undergoing Curative Tumor Resection. Journal of Cancer, 2019, 10(9):2057-2062.

[29] Chen MF, Chen PT, Kuan FC, Chen WC. The Predictive Value of Pretreatment Neutrophil-To-Lymphocyte Ratio in Esophageal Squamous Cell Carcinoma. Annals of Surgical Oncology, 2019, 26(1):190-199.

[30] Duan H, Zhang X, Wang FX, Cai MY, Ma GW, Yang H, Fu JH, Tan ZH, Meng YQ, Fu XY, Ma QL, Lin P. Prognostic role of neutrophil-lymphocyte ratio in operable esophageal squamous cell carcinoma. World Journal of Gastroenterology, 2015, 21(18):5591-5597.

[31] Gao GD, Sun B, Wang XB, Wang SM. Neutrophil to lymphocyte ratio as prognostic indicator for patients with esophageal squamous cell cancer. International Journal of Biological Markers, 2017, 32(4):E409-E414.

[32] Han FY, Liu YQ, Cheng SQ, Sun ZH, Sheng CC, Sun XY, Shang XM, Tian WJ, Wang XY, Li JM, Liu D, Wang Y, Zhang BC, Ju Y. Diagnosis and survival values of neutrophil-lymphocyte ratio (NLR) and red blood cell distribution width (RDW) in esophageal cancer. Clinica Chimica Acta, 2019, 488:150-158.

[33] Hirahara N, Matsubara T, Hayashi H, Takai K, Nakada S, Tajima Y. Prognostic Importance of Controlling Nutritional Status in Patients Undergoing Curative Thoracoscopic Esophagectomy for Esophageal Cancer. American Journal of Therapeutics, 2018, 25(5):E524-E532.

[34] Kosumi K, Baba Y, Ishimoto T, Harada K, Nakamura K, Ohuchi M, Kiyozumi Y, Izumi D, Tokunaga R, Taki K, Higashi T, Miyata T, Kurashige J, Hiyoshi Y, Iwagami S, Sakamoto Y, Miyamoto Y, Yoshida N, Watanabe M, Baba H. Neutrophil/lymphocyte ratio predicts the prognosis in esophageal squamous cell carcinoma patients. Surgery Today, 2016, 46(4):405-413.

[35] Lv Y, Zhang J, Liu Z, Tian Y, Liu F. A novel inflammation-based prognostic index for patients with esophageal squamous cell carcinoma: Neutrophil lymphocyte ratio/prealbumin ratio. Medicine (Baltimore), 2019, 98(7):e14562.

[36] Nakamura K, Yoshida N, Baba Y, Kosumi K, Uchihara T, Kiyozumi Y, Ohuchi M, Ishimoto T, Iwatsuki M, Sakamoto Y, Watanabe M, Baba H. Elevated preoperative neutrophil-to-lymphocytes ratio predicts poor prognosis after esophagectomy in T1 esophageal cancer. International Journal of Clinical Oncology, 2017, 22(3):469-475.

[37] Sharaiha RZ, Halazun KJ, Mirza F, Port JL, Lee PC, Neugut AI, Altorki NK, Abrams JA. Elevated Preoperative Neutrophil:Lymphocyte Ratio as a Predictor of Postoperative Disease Recurrence in Esophageal Cancer. Annals of Surgical Oncology, 2011, 18(12):3362-3369.

[38] Xiao Q, Zhang BH, Deng X, Wu J, Wang H, Wang YG, Wang WX. The Preoperative Neutrophil-To-Lymphocyte Ratio Is a Novel Immune Parameter for the Prognosis of Esophageal Basaloid Squamous Cell Carcinoma. Plos One, 2016, 11(12).

[39] Zhou XL, Li YQ, Zhu WG, Yu CH, Song YQ, Wang WW, He DC, Tao GZ, Tong YS. Neutrophil-to-lymphocyte ratio as a prognostic biomarker for patients with locally advanced esophageal squamous cell carcinoma treated with definitive chemoradiotherapy. Scientific Reports, 2017, 7.

[40] Arigami T, Okumura H, Matsumoto M, Uchikado Y, Uenosono Y, Kita Y, Owaki T, Mori S, Kurahara H, Kijima Y, Ishigami S, Natsugoe S. Analysis of the Fibrinogen and Neutrophil-Lymphocyte Ratio in Esophageal Squamous Cell Carcinoma A Promising Blood Marker of Tumor Progression and Prognosis. Medicine, 2015, 94(42).

[41] Lindenmann J, Fink-Neuboeck N, Avian A, Pichler M, Habitzruther M, Maier A, Smolle-Juettner FM. Preoperative Glasgow Prognostic Score as additional independent prognostic parameter for patients with esophageal cancer after curative esophagectomy. Ejso, 2017, 43(2):445-453.

[42] Ma QL, Liu WG, Jia R, Jiang F, Duan H, Lin P, Zhang LJ, Long H, Zhao HY, Ma GW. Inflammation-based prognostic system predicts postoperative survival of esophageal carcinoma patients with normal preoperative serum carcinoembryonic antigen and squamous cell carcinoma antigen levels. World Journal of Surgical Oncology, 2016, 14.

[43] Okuno T, Wakabayashi M, Kato K, Shinoda M, Katayama H, Igaki H, Tsubosa Y, Kojima T, Okabe H, Kimura Y, Kawano T, Kosugi S, Toh Y, Kato H, Nakamura K, Fukuda H, Ishikura S, Ando N, Kitagawa Y. Esophageal stenosis and the Glasgow Prognostic Score as independent factors of poor prognosis for patients with locally advanced unresectable esophageal cancer treated with chemoradiotherapy (exploratory analysis of JCOG0303). International Journal of Clinical Oncology, 2017, 22(6):1042-1049.

[44] Sugawara K, Mori K, Yagi K, Aikou S, Uemura Y, Yamashita H, Seto Y. Association of preoperative inflammation-based prognostic score with survival in patients undergoing salvage esophagectomy. Diseases of the Esophagus, 2018, 32(4).

[45] Vashist YK, Loos J, Dedow J, Tachezy M, Uzunoglu G, Kutup A, Yekebas EF, Izbicki JR. Glasgow Prognostic Score is a Predictor of Perioperative and Long-term Outcome in Patients with only Surgically Treated Esophageal Cancer. Annals of

Surgical Oncology, 2011, 18(4):1130-1138.

[46] Hirahara N, Matsubara T, Hayashi H, Takai K, Fujii Y, Tajima Y. Impact of inflammation-based prognostic score on survival after curative thoracoscopic esophagectomy for esophageal cancer. Ejso, 2015, 41(10):1308-1315.

[47] Kitagawa H, Namikawa T, Munekage M, Fujisawa K, Kawanishi Y, Kobayashi M, Hanazaki K. Preoperative patient-related factors associated with prognosis after esophagectomy for esophageal cancer. Esophagus, 2017, 14(4):360-365.

[48] Jomrich G, Paireder M, Gleiss A, Kristo I, Harpain L, Schoppmann SF. Comparison of Inflammation-Based Prognostic Scores in a Cohort of Patients with Resectable Esophageal Cancer. Gastroenterology Research and Practice, 2017.

[49] Kimura J, Kunisaki C, Makino H, Oshima T, Ota M, Oba M, Takagawa R, Kosaka T, Ono HA, Akiyama H, Endo I. Evaluation of the Glasgow Prognostic Score in patients receiving chemoradiotherapy for stage III and IV esophageal cancer. Diseases of the Esophagus, 2016, 29(8):1071-1080.

[50] Chen P, Fang M, Wan QY, Zhang XB, Song T, Wu SX. High-sensitivity modified Glasgow prognostic score (HS-mGPS) Is superior to the mGPS in esophageal cancer patients treated with chemoradiotherapy. Oncotarget, 2017, 8(59):99861-99870.

[51] Otowa Y, Nakamura T, Takiguchi G, Tomono A, Yamamoto M, Kanaji S, Imanishi T, Suzuki S, Tanaka K, Itoh T, Kakeji Y. Changes in modified Glasgow prognostic score after neoadjuvant chemotherapy is a prognostic factor in clinical stage II/III esophageal cancer. Diseases of the Esophagus, 2016, 29(2):146-151.

[52] Tian R, Zhang F, Sun P, Wu J, Yan H, Wu AR, Zhang M, Jiang YL, Lu YH, Xu QY, Zhan XH, Zhang RX, Qian LT, He J. The preoperative sensitive-modified Glasgow prognostic score is superior to the modified Glasgow prognostic score in predicting long-term survival for esophageal squamous cell carcinoma. Oncotarget, 2016, 7(41):67485-67494.

[53] Walsh SM, Casey S, Kennedy R, Ravi N, Reynolds JV. Does the Modified Glasgow Prognostic Score (mGPS) Have a Prognostic Role in Esophageal Cancer? Journal of Surgical Oncology, 2016, 113(7):732-737.

[54] Zhang P, Xi M, Li QQ, He LR, Liu SL, Zhao L, Shen JX, Liu MZ. The Modified Glasgow Prognostic Score Is an Independent Prognostic Factor in Patients with Inoperable Thoracic Esophageal Squamous Cell Carcinoma Undergoing Chemoradiotherapy. Journal of Cancer, 2014, 5(8):689-695.

[55] Sun P, Zhang F, Chen C, An X, Li YH, Wang FH, Zhu ZH. Comparison of the prognostic values of various nutritional parameters in patients with esophageal squamous cell carcinoma from Southern China. Journal of Thoracic Disease, 2013, 5(4):484-491.

[56] Chen S, Yang X, Feng JF. A novel inflammation-based prognostic score for patients with esophageal squamous cell carcinoma: the c-reactive protein/prognostic nutritional index ratio. Oncotarget, 2016, 7(38):62123-62132.

[57] Okadome K, Baba Y, Yagi T, Kiyozumi Y, Ishimoto T, Iwatsuki M, Miyamoto Y, Yoshida N, Watanabe M, Baba H. Prognostic Nutritional Index, Tumor-infiltrating Lymphocytes, and Prognosis in Patients with Esophageal Cancer. Ann Surg, 2018.

[58] Migita K, Matsumoto S, Wakatsuki K, Ito M, Kunishige T, Nakade H, Sho M. The Prognostic Significance of the Geriatric Nutritional Risk Index in Patients with Esophageal Squamous Cell Carcinoma. Nutrition and Cancer-an International Journal, 2018, 70(8):1237-1245.

[59] Zhang H, Guo XW, Yin XX, Liu YC, Ji SJ. Nomogram-Integrated C-Reactive Protein/Albumin Ratio Predicts Efficacy And Prognosis In Patients With Thoracic Esophageal Squamous Cell Carcinoma Receiving Chemoradiotherapy. Cancer Management and Research, 2019, 11:9459-9468.

[60] Otowa Y, Nakamura T, Yamamoto M, Kanaji S, Matsuda Y, Matsuda T, Oshikiri T, Sumi Y, Suzuki S, Kakeji Y. C-reactive protein to albumin ratio is a prognostic factor for patients with cStage II/III esophageal squamous cell cancer. Diseases of the Esophagus, 2017, 30(12).

[61] Liu XQ, Chen W, Qiao TK. Prognostic significance of serum C-reactive protein to albumin ratios in esophageal cancer patients receiving radical radiotherapy. International Journal of Clinical and Experimental Medicine, 2019, 12(6):7585-7592.

[62] Shao YJ, Ning ZH, Chen J, Geng YT, Gu WD, Huang J, Pei HL, Shen YP, Jiang JT. Prognostic nomogram integrated systemic inflammation score for patients with esophageal squamouscell carcinoma undergoing radical esophagectomy. Scientific Reports, 2015, 5.

[63] Liu DQ, Li FF, Jia WH. Cumulative scores based on plasma D-dimer and serum albumin levels predict survival in esophageal squamous cell carcinoma patients treated with transthoracic esophagectomy. Chinese Journal of Cancer, 2016, 35.

[64] Wang CY, Lee TF, Fang CH, Chou JH. Fuzzy Logic-Based Prognostic Score for Outcome Prediction in Esophageal Cancer. Ieee Transactions on Information Technology in Biomedicine, 2012, 16(6):1224-1230.

[65] Feng JF, Zhao Q, Chen QX. Prognostic Significance of Glasgow prognostic score in patients undergoing esophagectomy for esophageal squamous cell carcinoma. Saudi Journal of Gastroenterology, 2014, 20(1):48-53.

[66] Lindenmann J, Fink-Neuboeck N, Koesslbacher M, Pichler M, Stojakovic T, Roller RE, Maier A, Anegg U, Smolle J, Smolle-Juettner FM. The Influence of Elevated Levels of C-Reactive Protein and Hypoalbuminemia on Survival in Patients with Advanced Inoperable Esophageal Cancer Undergoing Palliative Treatment. Journal of Surgical Oncology, 2014, 110(6):645-650.

[67] Matsuda S, Takeuchi H, Kawakubo H, Fukuda K, Nakamura R, Takahashi T, Wada N, Saikawa Y, Omori T, Kitagawa Y. Cumulative Prognostic Scores Based on Plasma Fibrinogen and Serum Albumin Levels in Esophageal Cancer Patients Treated with Transthoracic Esophagectomy: Comparison with the Glasgow Prognostic Score. Annals of Surgical Oncology, 2015, 22(1):302-310.

[68] Liu XM, Li MH, Zhao F, Zhu YM, Luo YJ, Kong L, Zhu H, Zhang Y, Shi F, Yu JM. The lymphocyte-monocyte ratio predicts tumor response and survival in patients with locally advanced esophageal cancer who received definitive chemoradiotherapy. Oncotargets and Therapy, 2017, 10:871-877.

[69] Tian R, Yan H, Zhang F, Sun P, Wu AR, Zhang M, Jiang YL, Wu J, Lu YH, Xu QY, Zhan XH, Zhang RX, Qian LT, He J. Cumulative score based on preoperative plasma fibrinogen and serum C-reactive protein could predict long-term survival for esophageal squamous cell carcinoma. Oncotarget, 2016, 7(38):61533-61543.

[70] Nakamura M, Iwahashi M, Nakamori M, Ojima T, Katsuda M, Iida T, Hayata K, Kato T, Yamaue H. New prognostic score for the survival of patients with esophageal squamous cell carcinoma. Surg Today, 2014, 44(5):875-883.

[71] Han L, Song Q, Jia Y, Chen X, Wang C, Chen P, Min R, Cheng Y. The clinical significance of systemic inflammation score in esophageal squamous cell carcinoma. Tumour Biol, 2015, 37(3):3081-3090.

[72] Miyazaki T, Sakai M, Sohda M, Tanaka N, Yokobori T, Motegi Y, Nakajima M, Fukuchi M, Kato H, Kuwano H. Prognostic Significance of Inflammatory and Nutritional Parameters in Patients with Esophageal Cancer. Anticancer Res, 2016, 36(12):6557-6562.

Table 1. Subgroup analysis and meta analysis of 8 indicators in OS, CSS, and DFS.

	OS					CSS					DFS				
	N	**HR(95% CI), *P***	**I^2(%), *P***	**Begg's *P*, Egger's *P***	***P*-reg**	**N**	**HR(95% CI), *P***	**I^2(%), *P***	**Begg's *P*, Egger's *P***	***P*-reg**	**N**	**HR(95% CI), *P***	**I^2(%), *P***	**Begg's *P*, Egger's *P***	***P*-reg**
PNI															
Overall	11	1.51(1.36-1.68),<0.001	45.8, 0.048	0.036, 0.188											
Country															
China	4	1.45(1.27-1.64),<0.001	36.9, 0.190	0.497, 0.092	0.184										
Non-China	7	1.82(1.38-2.40),<0.001	51.4, 0.054	0.099, 0.006											
Sample size															
<255	7	1.69(1.19-2.40), 0.003	66.8, 0.006	0.099, 0.058	0.797										
≥255	4	1.52(1.34-1.72),<0.001	0.0, 0.949	0.174, 0.052											
Cut-off value															
<46	5	1.68(1.13-2.50), 0.010	59.5, 0.043	0.050, 0.432	0.774										
≥46	6	1.49(1.33-1.67),<0.001	39.9, 0.139	0.348, 0.288											
Treatment															
Surgery	7	1.46(1.20-1.78),<0.001	54.4, 0.041	0.752, 0.293	Ref										
Mixed	3	2.18(1.52-3.11),<0.001	0.0, 0.649	0.602, 0.448	0.139										
NR	1	1.50(1.16-1.93), NR	NR	NR	0.906										
Pathology															
SCC	9	1.56(1.39-1.76),<0.001	41.5, 0.091	0.061, 0.184	0.144										
Mixed	1	1.67(1.14-2.44), NR	NR	NR	0.231										
NR	1	1.09(0.80-1.49), NR	NR	NR	Ref										
Clinical stage															
0-III	5	1.62(1.41-1.86),<0.001	32.2, 0.207	0.050,<0.001	0.229										
0-IV	6	1.41(1.10-1.80), 0.006	52.4, 0.062	0.348, 0.687											
Follow-up															
<36	4	1.46(1.15-1.86), 0.002	53.4, 0.092	1.000, 0.523	0.962										
≥36	4	1.45(1.23-1.70),<0.001	46.1, 0.135	1.000, 0.801	Ref										
NR	3	2.26(1.63-3.14),<0.001	0.0, 0.988	0.602, 0.337	0.014										
Age															
<63.4	4	1.45(1.27-1.64),<0.001	36.9, 0.190	0.497, 0.092	Ref										
≥63.4	6	1.77(1.31-2.41),<0.001	55.0, 0.049	0.039, 0.016	0.270										
NR	1	2.21(1.28-3.82), NR	NR	NR	0.249										
Sex ratio															

<4.75	5	1.46(1.29-1.66),<0.001	25.1, 0.254	0.624, 0.545	0.253										
≥4.75	6	1.84(1.34-2.53),<0.001	59.1, 0.032	0.091, 0.011											
NLR															
Overall	34	1.43(1.30-1.58),<0.001	61.7,<0.001	0.113, 0.428		8	1.21(1.04-1.41), 0.011	43.4, 0.089	0.621, 0.695		7	1.39(1.10-1.75), 0.005	60.9, 0.018	0.453, 0.344	
Country															
China	23	1.43(1.30-1.57),<0.001	51.5, 0.002	0.107, 0.399	0.883	4	1.15(0.97-1.36), 0.117	38.8, 0.179	0.174, 0.971	0.436	5	1.22(1.05-1.42), 0.010	0.0, 0.514	0.050, 0.062	0.018
Non-China	11	1.45(1.06-1.98), 0.022	75.5,<0.001	0.484, 0.513		4	1.42(1.06-1.90), 0.020	49.8, 0.113	0.497, 0.376		2	2.43(1.69-3.49),<0.001	0.0, 0.604	NR	
Sample size															
<297	18	1.45(1.19-1.76),<0.001	65.6,<0.001	0.088, 0.192	0.965	2	0.95(0.59-1.54), 0.848	43.6, 0.183	NR	0.395	4	1.56(0.95-2.58), 0.080	78.9, 0.003	0.174, 0.316	0.553
≥297	15	1.42(1.27-1.58),<0.001	60.2, 0.001	0.347, 0.809	Ref	6	1.24(1.06-1.45), 0.006	47.5, 0.090	0.091, 0.138		3	1.29(1.08-1.54), 0.005	0.0, 0.799	0.117, 0.089	
NR	1	1.84(1.21-2.83), NR	NR	NR	0.466	NR	NR	NR	NR		NR	NR	NR	NR	
Cut-off value															
<2.5	16	1.38(1.20-1.58),<0.001	56.9, 0.003	0.072, 0.082	0.563	3	1.43(1.04-1.97), 0.030	66.5, 0.051	0.602, 0.268	0.493	4	1.34(0.94-1.91), 0.103	69.2, 0.021	1.000, 0.704	0.763
≥2.5	18	1.48(1.28-1.71),<0.001	62.5,<0.001	0.733, 0.623		5	1.16(0.98-1.37), 0.084	21.9, 0.275	0.142, 0.737		3	1.47(1.03-2.11), 0.034	61.8, 0.073	0.117, 0.377	
Treatment															
Surgery	24	1.32(1.19-1.48),<0.001	56.9,<0.001	0.215, 0.290	Ref	8	1.21(1.04-1.41), 0.010	43.4, 0.089	0.621, 0.695		7	1.39(1.10-1.75), 0.005	60.9, 0.018	0.453, 0.344	
CRT	3	1.79(1.51-2.13),<0.001	0.0, 0.704	0.602, 0.960	0.090	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mixed	7	1.73(1.51-1.99),<0.001	39.3, 0.130	0.176, 0.779	0.062	NR	NR	NR	NR		NR	NR	NR	NR	
Pathology															
SCC	27	1.42(1.28-1.57),<0.001	56.0,<0.001	0.084, 0.517	0.683	8	1.21(1.04-1.41), 0.011	43.4, 0.089	0.621, 0.695		5	1.22(1.05-1.42), 0.010	0.0, 0.514	0.050, 0.062	0.018
Mixed	4	1.75(0.84-3.66), 0.137	87.9,<0.001	1.000, 0.661	0.420	NR	NR	NR	NR	NR	2	2.43(1.69-3.49),<0.001	0.0, 0.604	NR	
NR	3	1.36(1.13-1.65), 0.002	0.0, 0.509	0.602, 0.452	Ref	NR	NR	NR	NR		NR	NR	NR	NR	
Clinical stage															
0-III	22	1.31(1.22-1.41),<0.001	43.0, 0.018	0.019, 0.039	0.262	6	1.12(0.96-1.32), 0.159	30.4, 0.207	0.573, 0.701	0.083	5	1.35(1.15-1.57),<0.001	36.4, 0.179	0.624, 0.229	0.963
0-IV	12	1.56(1.28-1.89),<0.001	71.1,<0.001	0.784, 0.600		2	1.80(1.24-2.60), 0.002	0.0, 0.907	0.317, NR		2	1.40(0.55-3.57), 0.486	89.0, 0.003	0.317, NR	
Follow-up															
<37	12	1.60(1.34-1.91),<0.001	60.5, 0.003	0.493, 0.485	0.079	2	1.80(1.24-2.60), 0.002	0.0, 0.907	0.317, NR	0.105	2	1.40(0.55-3.57), 0.486	89.0, 0.003	0.317, NR	0.963
≥37	10	1.26(1.15-1.38),<0.001	45.4, 0.058	0.531, 0.844	Ref	3	1.11(0.73-1.69), 0.623	67.1, 0.048	0.602, 0.534	0.740	5	1.35(1.15-1.57),<0.001	36.4, 0.179	0.624, 0.229	
NR	12	1.45(1.20-1.76),<0.001	64.8, 0.001	0.217, 0.832	0.307	3	1.06(0.84-1.34), 0.614	0.0, 0.712	0.117, 0.166	Ref	NR	NR	NR	NR	
Age															
<61.1	15	1.37(1.22-1.53),<0.001	53.9, 0.007	0.083, 0.446	Ref	3	1.28(1.02-1.61), 0.033	40.9, 0.184	0.602, 0.932		4	1.28(1.09-1.50), 0.003	0.0, 0.919	0.174, 0.075	Ref
≥61.1	11	1.45(1.16-1.82), 0.001	70.3,<0.001	0.697, 0.636	0.706	NR	NR	NR	NR	0.759	2	1.40(0.55-3.57), 0.486	89.0, 0.003	0.317, NR	0.775
NR	8	1.56(1.16-2.10), 0.003	62.9, 0.009	0.805, 0.875	0.461	5	1.20(0.88-1.62), 0.246	53.4, 0.072	1.000, 0.651		1	2.76(1.50-5.03), NR	NR	NR	0.152
Sex ratio															
<5.12	17	1.38(1.22-1.56),<0.001	62.3,<0.001	0.510, 0.856	0.458	7	1.14(0.96-1.34), 0.129	35.6, 0.157	0.453, 0.417	0.287	6	1.30(1.26-1.50),<0.001	48.4, 0.085	0.573, 0.960	0.123

≥5.12	17	1.52(1.27-1.81),<0.001	62.8,<0.001	0.021, 0.286		1	1.59(1.13-2.24), NR	NR	NR	1	2.76(1.50-5.03), NR	NR	NR	
PLR														
Overall	19	1.26(1.18-1.35),<0.001	29.8, 0.108	0.054, 0.108						5	1.30(1.12-1.51),<0.001	33.0, 0.202	0.142, 0.472	
Country														
China	15	1.26(1.17-1.35),<0.001	42.1, 0.043	0.125, 0.121	0.571					5	1.30(1.12-1.51),<0.001	33.0, 0.202	0.142, 0.472	NR
Non-China	4	1.40(1.07-1.83), 0.016	0.0, 0.854	1.000, 0.771						NR	NR	NR	NR	
Sample size														
<303	10	1.38(1.18-1.62),<0.001	25.5, 0.209	0.245, 0.157	0.341					2	0.99(0.71-1.39), 0.958	0.0, 0.682	0.602, 0.463	0.174
≥303	9	1.24(1.15-1.34),<0.001	33.7, 0.148	0.297, 0.206						3	1.39(1.18-1.64),<0.001	24.5, 0.266	NR	
Cut-off value														
<143	10	1.24(1.14-1.35),<0.001	11.7, 0.335	0.006, 0.001	0.567					3	1.39(1.18-1.64),<0.001	24.5, 0.266	NR	0.174
≥143	9	1.33(1.17-1.52),<0.001	44.7, 0.071	1.000, 0.858						2	0.99(0.71-1.39), 0.958	0.0, 0.682	0.602, 0.463	
Treatment														
Surgery	15	1.24(1.16-1.33),<0.001	24.2, 0.186	0.458, 0.553	0.079					5	1.30(1.12-1.51),<0.001	33.0, 0.202	0.142, 0.472	NR
Mixed	4	1.61(1.26-2.06),<0.001	1.6, 0.384	0.174, 0.086						NR	NR	NR	NR	
Pathology														
SCC	17	1.27(1.19-1.37),<0.001	33.2, 0.091	0.070, 0.122	0.432					5	1.30(1.12-1.51),<0.001	33.0, 0.202	0.142, 0.472	
Mixed	1	1.55(0.95-2.59), NR	NR	NR	0.356					NR	NR	NR	NR	NR
NR	1	1.12(0.87-1.43), NR	NR	NR	Ref					NR	NR	NR	NR	
Clinical stage														
0-III	15	1.27(1.18-1.36),<0.001	34.7, 0.091	0.033, 0.039	0.733					4	1.34(1.15-1.57),<0.001	37.6, 0.187	0.497, 0.709	0.461
0-IV	4	1.21(0.94-1.57), 0.139	24.5, 0.265	0.497, 0.205						1	1.05(0.69-1.60), NR	NR	NR	
Follow-up														
<39	4	1.17(1.01-1.36), 0.041	18.8, 0.296	0.497, 0.311	Ref					1	1.05(0.69-1.60), NR	NR	NR	0.461
≥39	8	1.19(1.09-1.30),<0.001	0.0, 0.974	0.458, 0.520	0.855					4	1.34(1.15-1.57),<0.001	37.6, 0.187	0.497, 0.709	
NR	7	1.71(1.46-2.02),<0.001	0.0, 0.682	0.293, 0.441	0.004					NR	NR	NR	NR	
Age														
<61.2	12	1.26(1.17-1.35),<0.001	41.5, 0.065	0.100, 0.097	Ref					4	1.34(1.15-1.57),<0.001	37.6, 0.187	0.497, 0.709	0.461
≥61.2	6	1.33(1.10-1.61), 0.003	21.9, 0.269	0.348, 0.470	0.698					1	1.05(0.69-1.60), NR	NR	NR	
NR	1	1.27(0.76-2.12), NR	NR	NR	0.994					NR	NR	NR	NR	
Sex ratio														
<4.55	8	1.22(1.12-1.33),<0.001	0.0, 0.863	1.000, 0.810	0.265					4	1.34(1.15-1.57),<0.001	37.6, 0.187	0.497, 0.709	0.461
≥4.55	11	1.41(1.17-1.69),<0.001	51.4, 0.024	0.102, 0.213						1	1.05(0.69-1.60), NR	NR	NR	
LMR														
Overall	13	1.37(1.14-1.65), 0.001	84.9,<0.001	0.028, 0.167						6	1.08(0.85-1.39), 0.522	79.8,<0.001	0.573, 0.838	

Country										
China	12	1.35(1.11-1.63), 0.002	85.7,<0.001	0.028, 0.229	0.525	6	1.08(0.85-1.39), 0.522	79.8,<0.001	0.573, 0.838	NR
Non-China	1	1.87(1.09-3.23), NR	NR	NR		NR	NR	NR	NR	
Sample size										
<280	7	1.86(1.36-2.55),<0.001	75.4,<0.001	0.881, 0.609	0.006	3	1.44(1.19-1.76),<0.001	0.0, 0.686	0.117, 0.290	0.085
≥280	6	1.09(0.97-1.22), 0.168	54.1, 0.053	0.348, 0.357		3	0.81(0.54-1.20), 0.296	87.0,<0.001	0.117, 0.013	
Cut-off value										
<3.57	6	1.65(1.11-2.47), 0.014	91.1,<0.001	0.851, 0.191	0.174	4	1.18(1.08-1.29),<0.001	49.5, 0.115	0.042, 0.025	0.034
≥3.57	7	1.17(0.97-1.42), 0.110	71.1, 0.002	0.293, 0.627		2	0.65(0.38-1.11), 0.116	73.7, 0.051	NR	
Treatment										
Surgery	9	1.20(1.02-1.41), 0.033	62.2, 0.007	0.144, 0.496	Ref	4	1.00(0.61-1.62), 0.984	86.3,<0.001	1.000, 0.995	
CCRT	1	3.60(2.66-4.88), NR	NR	NR	0.006	NR	NR	NR	NR	0.651
Mixed	3	1.36(1.01-1.83), 0.045	73.1, 0.024	0.117, 0.179	0.539	2	1.14(1.04-1.25), 0.005	12.4, 0.285	NR	
Pathology										
SCC	13	1.37(1.14-1.65), 0.001	84.9,<0.001	0.028, 0.167	NR	6	1.08(0.85-1.39), 0.522	79.8,<0.001	0.573, 0.838	NR
Mixed	NR	NR	NR	NR		NR	NR	NR	NR	
Clinical stage										
0-III	11	1.46(1.20-1.77),<0.001	84.7,<0.001	0.010, 0.055	0.176	4	1.15(0.92-1.45), 0.219	73.5, 0.010	0.174, 0.779	0.484
0-IV	2	0.93(0.39-2.21), 0.875	90.2, 0.001	0.317, NR		2	0.84(0.28-2.54), 0.754	92.2,<0.001	0.317, NR	
Follow-up										
<39	4	1.67(0.77-3.65), 0.198	94.3,<0.001	1.000, 0.505	0.429	2	0.89(0.26-3.02), 0.848	93.5,<0.001	0.317, NR	Ref
≥39	7	1.20(1.09-1.32),<0.001	0.0, 0.524	0.004, 0.002	0.891	3	1.15(0.79-1.66), 0.466	78.2, 0.010	0.117, 0.295	0.661
NR	2	1.12(1.02-1.23), 0.014	0.0, 0.515	0.317, NR	Ref	1	1.12(1.02-1.24), NR	NR	NR	0.767
Age										
<61.5	7	1.16(1.08-1.24),<0.001	12.9, 0.331	0.024, 0.044	Ref	4	1.17(0.92-1.50), 0.208	75.0, 0.007	0.174, 0.723	0.104
≥61.5	4	1.59(0.67-3.93), 0.312	94.3,<0.001	0.497, 0.692	0.373	1	0.47(0.28-0.78), NR	NR	NR	Ref
NR	2	1.46(1.12-1.90), 0.005	5.1, 0.305	0.317, NR	0.544	1	1.33(0.99-1.79), NR	NR	NR	0.119
Sex ratio										
<4.32	7	1.21(1.10-1.33),<0.001	21.5, 0.266	0.004, 0.005	0.575	3	1.15(0.79-1.66), 0466	78.2, 0.010	0.117, 0.295	0.708
≥4.32	6	1.50(0.91-2.46), 0.109	93.1,<0.001	0.851, 0.462		3	0.99(0.60-1.65), 0.969	87.1,<0.001	0.602, 0.808	
SII										
Overall	7	1.46(1.30-1.65),<0.001	41.0, 0.118	0.099, 0.113						
Country										
China	6	1.53(1.27-1.85),<0.001	50.5, 0.073	0.091, 0.082	0.890					
Non-China	1	1.65(0.74-3.96), NR	NR	NR						

Sample size														
<298	3	2.31(1.61-3.33),<0.001	0.0, 0.655	0.602, 0.400	0.047									
≥298	4	1.38(1.22-1.57),<0.001	0.0, 0.481	0.497, 0.490										
Cut-off value														
<410	3	1.31(1.11-1.54), 0.001	0.0, 0.372	0.117, 0.052	0.140									
≥410	4	1.67(1.40-1.99),<0.001	30.6, 0.229	0.497, 0.595										
Treatment														
Surgery	6	1.45(1.28-1.64),<0.001	45.0, 0.106	0.188, 0.204	0.428									
CRT	1	2.29(0.98-5.30), NR	NR	NR										
Pathology														
SCC	6	1.53(1.27-1.85),<0.001	50.5, 0.073	0.091, 0.082	0.890									
Mixed	1	1.65(0.74-3.96), NR	NR	NR										
Clinical stage														
0-III	5	1.40(1.23-1.59),<0.001	0.0, 0.435	0.327, 0.181	0.068									
0-IV	2	2.32(1.55-3.48),<0.001	0.0, 0.358	0.317, NR										
Follow-up														
<36	1	2.29(0.98-5.30), NR	NR	NR	0.469									
≥36	4	1.54(1.20-1.96), 0,001	66.6, 0.029	0.174, 0.098	0.908									
NR	2	1.46(1.08-1.98), 0.013	0.0, 0.771	0.317, NR	Ref									
Age														
<63.0	3	1.37(1.19-1.58),<0.001	16.6, 0.301	0.602, 0.607	Ref									
≥63.0	2	2.32(1.55-3.48),<0.001	0.0, 0.358	0.317, NR	0.084									
NR	2	1.53(1.13-2.06), 0.006	0.0, 0.319	0.317, NR	0.580									
Sex ratio														
<4.55	3	1.40(1.20-1.64),<0.001	46.1, 0.156	0.602, 0.475	0.646									
≥4.55	4	1.55(1.29-1.87),<0.001	48.0, 0.123	0.174, 0.468										
GPS														
Overall	15	2.35(1.99-2.76),<0.001	36.5, 0.078	0.729, 0.838		5	1.64(1.33-1.94),<0.001	45.5, 0.119	0.624, 0.905		5	2.44(1.28-4.67), 0.007	57.5, 0.052	1.000, 0.751	
Country														
China	4	2.23(1.57-3.17),<0.001	7.5, 0.356	0.497, 0.323	0.952	4	1.66(1.48-1.87),<0.001	47.4, 0.812	0.734, 0432	0.246	1	2.75(0.37-20.31), NR	NR	NR	0.931
Non-China	11	2.38(1.98-2.86),<0.001	46.5, 0.044	0.484, 0.699		1	2.53(1.49-4.28), NR	NR	NR		4	2.43(1.17-5.06), 0.017	68.0, 0.025	0.497, 0.781	
Sample size														
<237	9	2.47(1.98-3.07),<0.001	48.5, 0.050	0.835, 0.944	0.653	1	2.53(1.49-4.28), NR	NR	NR	0.246	3	3.11(2.03-4.78),<0.001	0.0, 0.399	0.602, 0.499	0.108
≥237	6	2.21(1.73-2.82),<0.001	17.5, 0.300	0.851, 0.814		4	1.66(1.48-1.87),<0.001	47.4, 0.812	0.734, 0432		2	1.06(0.53-2.14), 0.867	0.0, 0.320	NR	
Cut-off value														

1-2 VS 0	7	2.49(1.95-3.18),<0.001	39.0, 0.132	0.293, 0.232	0.821	2	1.48(1.25-1.77),<0.001	0.0, 0.801	NR	0.169	1	4.92(2.12-11.64), NR	NR	NR	0.303
2 VS 0	8	2.24(1.80-2.78),<0.001	40.6, 0.108	0.805, 0.553		3	1.89(1.62-2.22),<0.001	42.5, 0.829	1.000, 0.861		4	1.95(1.30-2.93), 0.001	47.5, 0.126	0.497, 0.866	
Treatment															
Surgery	8	2.16(1.73-2.70),<0.001	52.2, 0.041	0.621, 0.575	Ref	5	1.64(1.33-1.94),<0.001	45.5, 0.119	0.624, 0.905		2	1.06(0.53-2.14), 0.867	0.0, 0.320	0.317, NR	Ref
CRT	2	2.81(1.37-5.76), 0..005	76.1, 0.041	NR	0.449	NR	NR	NR	NR	NR	1	2.53(1.49-4.28), NR	NR	NR	0.192
Mixed	5	2.42(1.73-3.73),<0.001	0.0, 0.786	0.624, 0.364	0.730	NR	NR	NR	NR		2	4.72(2.24-9.95),<0.001	0.0, 0.843	NR	0.104
Pathology															
SCC	5	2.17(1.59-2.96),<0.001	40.6, 0.151	0.624, 0.620	0.706	5	1.64(1.33-1.94),<0.001	45.5, 0.119	0.624, 0.905		2	2.54(1.53-4.23),<0.001	0.0, 0.936	NR	0.945
Mixed	8	2.65(2.12-3.31),<0.001	44.3, 0.083	0.621, 0.847	0.342	NR	NR	NR	NR	NR	3	2.50(0.74-8.47), 0.141	78.1, 0.010	0.602, 0.680	
NR	2	1.89(1.31-2.74), 0.001	0.0, 0.786	NR	Ref	NR	NR	NR	NR		NR	NR	NR	NR	
Clinical stage															
0-III	4	2.16(1.63-2.85),<0.001	0.0, 0.511	0.174, 0.201	0.741	4	1.66(1.48-1.87),<0.001	47.4, 0.812	0.734, 0432	0.246	NR	NR	NR	NR	NR
0-IV	11	2.45(2.00-3.00),<0.001	47.9, 0.038	0.938, 0.933		1	2.53(1.49-4.28), NR	NR	NR		5	2.44(1.28-4.67), 0.007	57.5, 0.052	1.000, 0.751	
Follow-up															
<40	5	3.30(2.16-5.05),<0.001	16.0, 0.312	0.624, 0.701	0.027	1	1.63(1.16-2.29), NR	NR	NR	0.567	2	4.72(2.24-9.95),<0.001	0.0, 0.843	NR	0.104
≥40	4	1.56(1.11-2.20), 0.011	21.0, 0.284	0.497, 0.860	Ref	3	1.73(1.53-1.97),<0.001	69.2, 0.889	1.000, 0.731	0.416	2	1.06(0.53-2.14), 0.867	0.0, 0.320	0.317, NR	Ref
NR	6	2.51(2.04-3.08),<0.001	3.8, 0.392	0.851, 0.847	0.052	1	1.18(0.64-2.17), NR	NR	NR	Ref	1	2.53(1.49-4.28), NR	NR	NR	0.192
Age															
<62.1	5	2.15(1.66-2.78),<0.001	0.0, 0.490	0.050, 0.074	0.821	4	1.72(1.53-1.94),<0.001	54.6, 0.831	1.000, 0.720		1	2.75(0.37-20.31), NR	NR	NR	0.931
≥62.1	8	2.46(1.65-3.68),<0.001	59.6, 0.015	0.805, 0.690	0.632	NR	NR	NR	NR	0.369	4	2.43(1.17-5.06), 0.017	68.0, 0.025	0.497, 0.781	
NR	2	2.03(1.15-3.58), 0.014	0.0, 0.972	0.317, NR	Ref	1	1.18(0.64-2.17), NR	NR	NR		NR	NR	NR	NR	
Sex ratio															
<5.48	8	2.51(1.70-3.70),<0.001	51.9, 0.042	0.322, 0.602	0.690	1	1.63(1.16-2.29), NR	NR	NR	0.893	3	2.23(0.64-7.81), 0.211	76.3, 0.015	0.602, 0.826	0.724
≥5.48	7	2.25(1.80-2.82),<0.001	17.0, 0.300	0.881, 0.572		4	1.71(1.51-1.93),<0.001	62.3, 0.852	0.734, 0.954		2	2.66(1.62-4.37),<0.001	0.0, 0.560	0.317, NR	
mGPS															
Overall	14	1.69(1.49-1.92),<0.001	48.4, 0.022	0.702, 0.354											
Country															
China	8	1.90(1.47-2.46),<0.001	63.2, 0.008	0.083, 0.107	0.370										
Non-China	6	1.52(1.12-2.06), 0.007	10.9, 0.346	0.348, 0.795											
Sample size															
<212	6	2.50(1.91-3.28),<0.001	0.0, 0.652	0.348, 0.249	0.014										
≥212	8	1.52(1.31-1.75),<0.001	40.1, 0.111	0.805, 0.893											
Cut-off value															
1-2 VS 0	9	1.56(1.35-1.81),<0.001	4.7, 0.077	1.000, 0.736	0.092										
2 VS 0	5	2.23(1.70-2.92),<0.001	31.5, 0.212	0.624, 0.943											

Treatment					
Surgery	8	1.40(1.17-1.68),<0.001	31.2, 0.179	0.805, 0.577	Ref
RT	2	2.12(1.26-3.57), 0.005	73.3, 0.053	NR	0.138
Mixed	4	2.56(1.81-3.62),<0.001	0.0, 0.824	1.000, 0.888	0.030
Pathology					
SCC	11	1.88(1.48-2.40),<0.001	56.7, 0.010	0.815, 0.222	0.383
AD	1	1.24(0.69-2.22), NR	NR	NR	0.932
Mixed	1	1.17(0.53-2.60), NR	NR	NR	Ref
NR	1	1.82(1.17-2.83), NR	NR	NR	0.502
Clinical stage					
0-III	9	1.64(1.26-2.13),<0.001	50.9, 0.038	0.532, 0.227	0.314
0-IV	5	1.89(1.56-2.28),<0.001	38.7, 0.163	1.000, 0.475	
Follow-up					
<39	4	1.56(1.28-1.91),<0.001	0.0, 0.533	0.497, 0.066	Ref
≥39	6	1.64(1.18-2.26), 0.003	54.2, 0.053	0.188, 0.166	0.714
NR	4	2.66(1.98-3.59),<0.001	0.0, 0.783	0.497, 0.550	0.026
Age					
<61.7	8	1.90(1.47-2.46),<0.001	63.2, 0.008	0.083, 0.107	0.370
≥61.7	6	1.52(1.12-2.06), 0.007	10.9, 0.346	0.348, 0.795	
Sex ratio					
<4.91	7	1.77(1.32-2.38),<0.001	64.0, 0.011	0.652, 0.409	0.930
≥4.91	7	1.81(1.44-2.29),<0.001	25.4, 0.235	0.652, 0.680	
CAR					
Overall	10	1.84(1.60-2.10),<0.001	41.8, 0.079	0.531, 0.809	
Country					
China	5	1.90(1.50-2.41),<0.001	55.1, 0.063	1.000, 0.692	0.415
Non-China	4	1.58(1.13-2.20), 0.008	40.9, 0.166	0.497, 0.377	Ref
NR	1	2.46(1.18-5.13), NR	NR	NR	0.360
Sample size					
<283	5	2.06(1.59-2.66),<0.001	0.0, 0.585	0.142, 0.143	0.396
≥283	4	1.71(1.26-2.31), 0.001	65.4, 0.021	0.174, 0.411	Ref
NR	1	2.46(1.18-5.13), NR	NR	NR	0.406
Cut-off value					
<0.13	4	1.63(1.35-1.96),<0.001	0.0, 0.443	0.174, 0.185	0.490
≥0.13	5	2.19(1.78-2.69),<0.001	43.2, 0.133	0.142, 0.271	0.230

NR	1	1.15(0.56-2.70), NR	NR	NR	Ref
Treatment					
Surgery	4	1.79(1.28-2.50), 0.001	62.4, 0.047	0.497, 0.432	0.963
RT	1	2.46(1.18-5.13), NR	NR	NR	0.516
Mixed	5	1.71(1.39-2.11),<0.001	36.8, 0.176	1.000, 0.632	Ref
Pathology					
SCC	6	1.70(1.44-2.01),<0.001	21.2, 0.274	0.851, 0.586	0.535
Mixed	2	1.38(0.63-3.03), 0.427	67.2, 0.081	NR	Ref
NR	2	2.44(1.86-3.20),<0.001	0.0, 0.981	NR	0.134
Clinical stage					
0-III	5	2.01(1.69-2.39),<0.001	33.5, 0.198	0.624, 0.603	0.230
0-IV	4	1.50(1.19-1.90), 0.001	39.4, 0.175	1.000, 0.791	Ref
NR	1	2.46(1.18-5.13), NR	NR	NR	0.332
Follow-up					
<40	2	1.53(1.25-1.89),<0.001	0.0, 0.390	0.317, NR	Ref
≥40	2	1.56(0.58-4.16), 0.377	84.7, 0.010	0.317, NR	0.405
NR	6	2.10(1.65-2.68), 0.001	0.0, 0.693	0.348, 0.261	0.213
Age					
<62.2	5	1.90(1.50-2.41),<0.001	55.1, 0.063	1.000, 0.692	0.415
≥62.2	4	1.58(1.13-2.20), 0.008	40.9, 0.166	0.497, 0.377	Ref
NR	1	2.46(1.18-5.13), NR	NR	NR	0.360
Sex ratio					
<5.5	4	1.53(1.26-1.85),<0.001	32.8, 0.216	0.497, 0.875	Ref
≥5.5	5	2.21(1.81-2.70),<0.001	0.0, 0.471	0.014, 0.048	0.045
NR	1	2.46(1.18-5.13), NR	NR	NR	0.285

Abbreviations: OS, overall survival; CSS, cancer-specific survival; DFS, disease-free survival; EC, esophageal carcinoma; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; CAR, c-reactive protein-to-albumin ratio; SII, systemic inflammation index; PNI, prognostic nutritional index; GPS, Glasgow Prognostic Score; mGPS, modified Glasgow Prognostic Score; Ref, reference; P-reg, the P-value of meta regression; NR, not reported.

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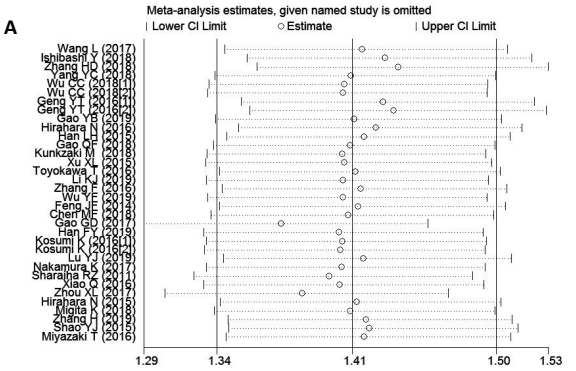
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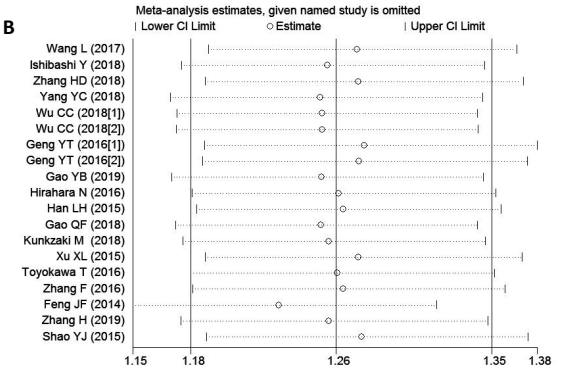
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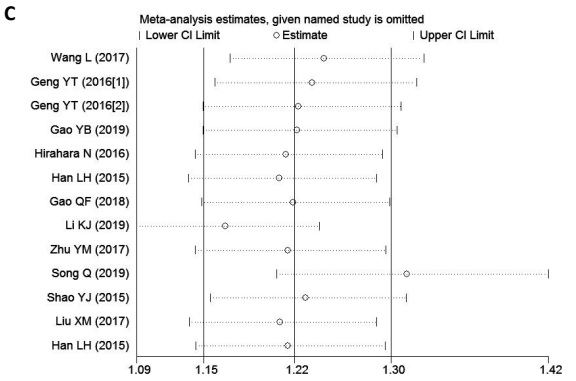
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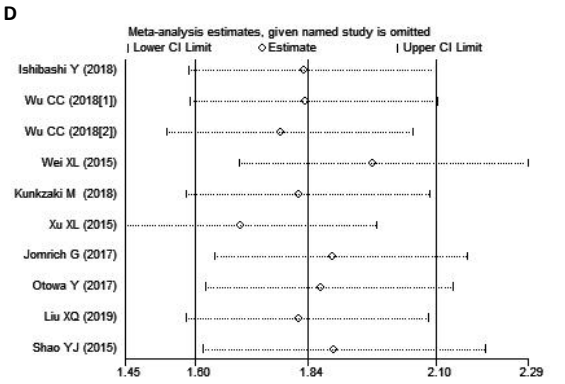
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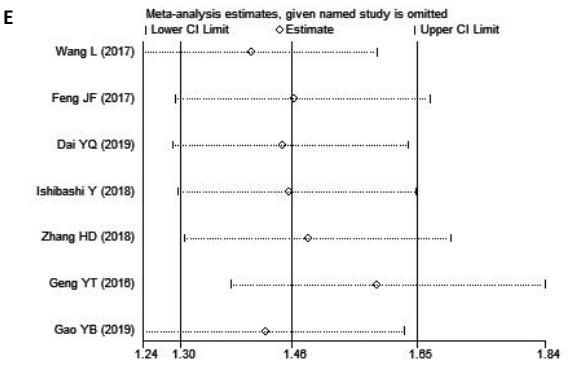
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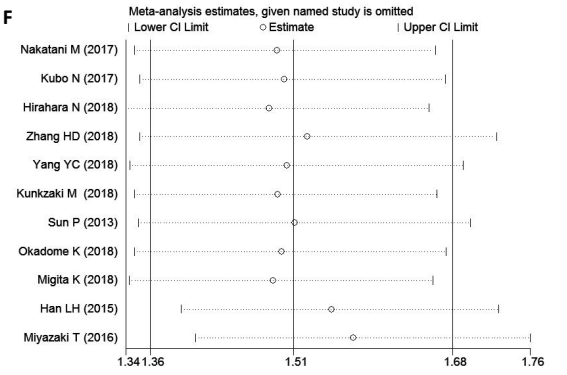
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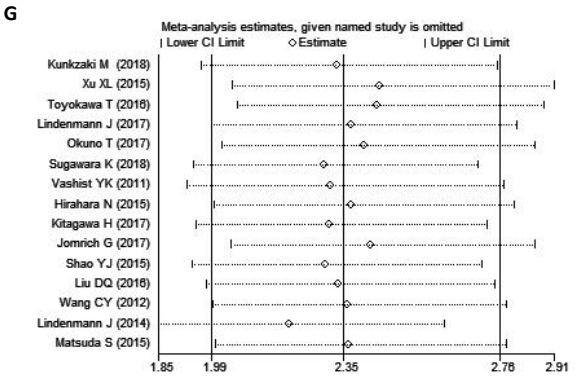
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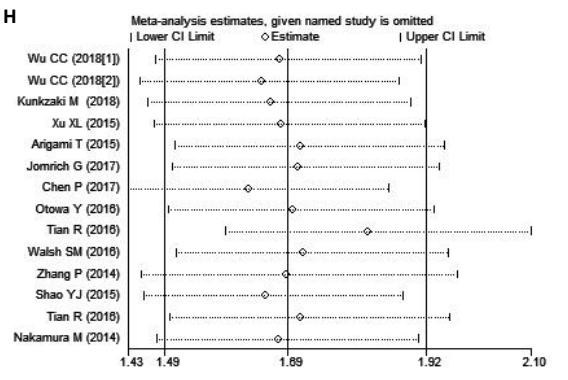
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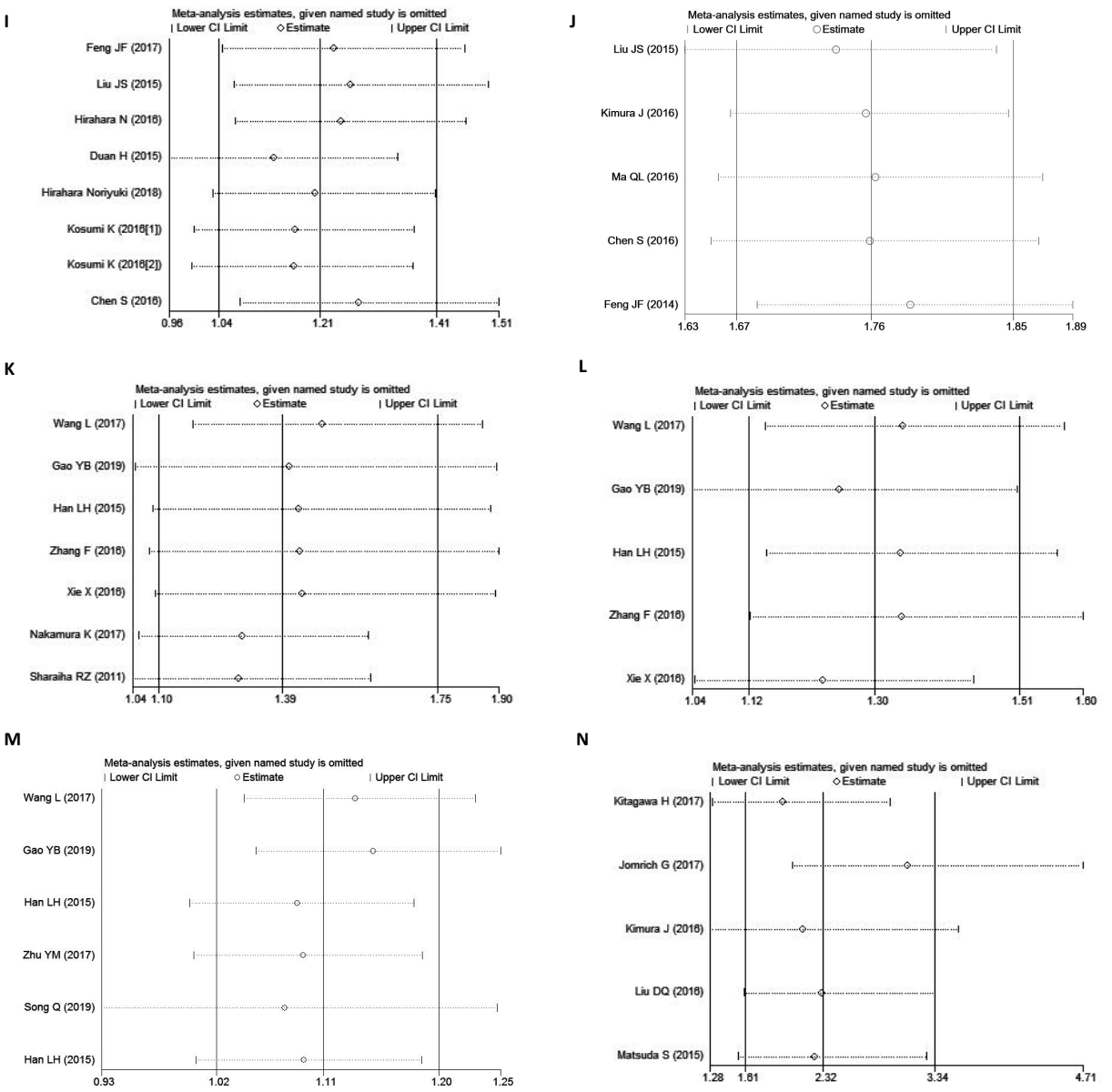

Figure 1. Sensitivity analyses of HR for 8 indicators in OS, CSS and DFS.
(A)NLR-OS; (B) PLR-OS; (C) LMR-OS; (D) CAR-OS; (E) SII-OS; (F) PNI-OS; (G) GPS-OS; (H) mGPS-OS; (I) NLR-CSS; (J) GPS-CSS; (K) NLR-DFS; (L) PLR-DFS; (M) LMR-DFS; (N) GPS-DFS.

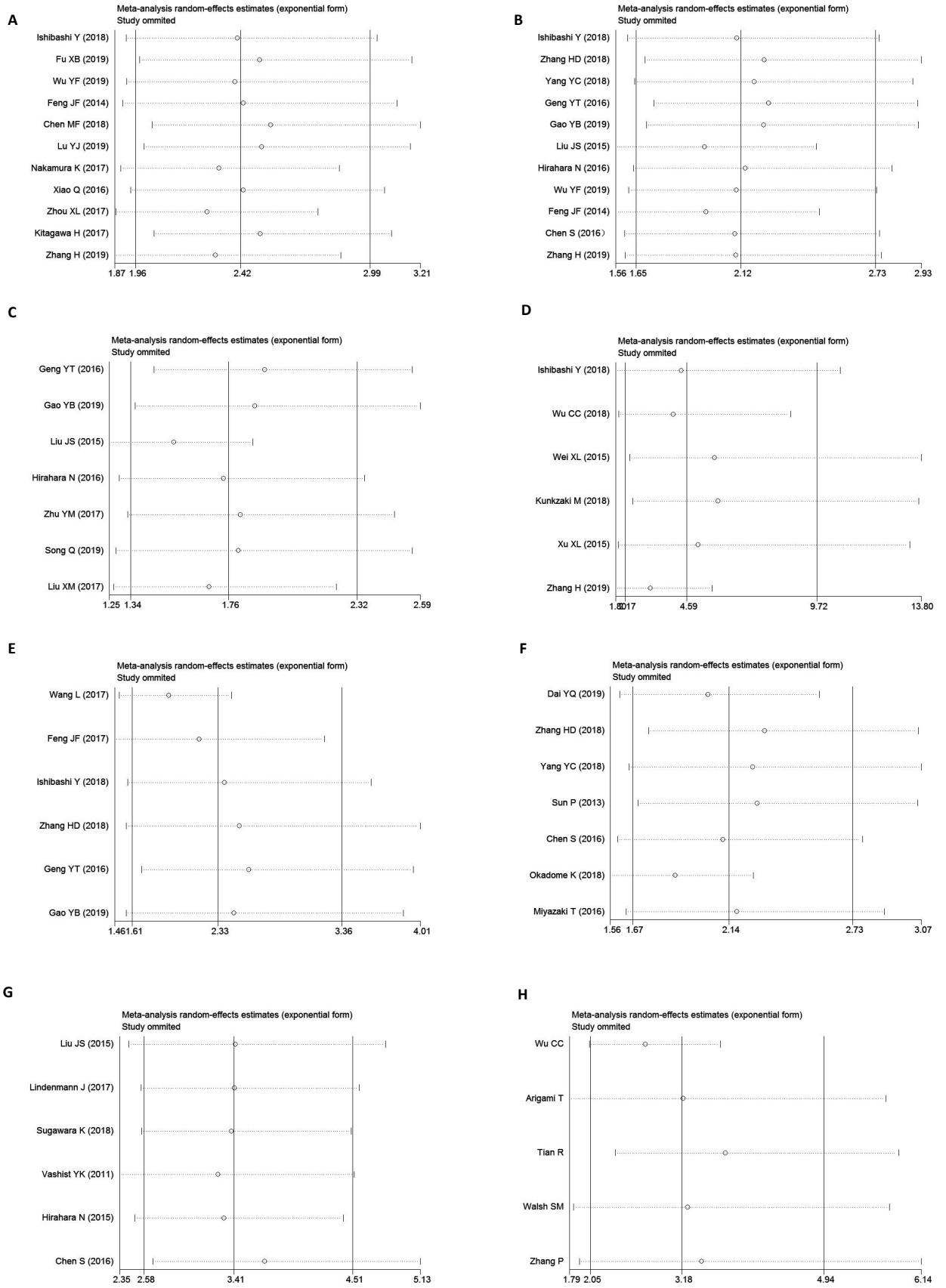

Figure 2. Sensitivity analyses of DOR for 8 indicators in 5-year OS of EC.
(A) NLR; (B) PLR; (C) LMR; (D) CAR; (E) SII; (F) PNI; (G) GPS; (H) mGPS;

Table 1. Subgroup and meta regression of sensitivity and specificity of prognostic indicators.

Category	NO. of Trails	Sensitivity (95%)	I^2(%), *P*	*P*-reg	Specificity (95%)	I^2(%), *P*	*P*-reg
SII							
Overall	6	0.61(0.48-0.73)	96.2, <0.001		0.60(0.45-0.73)	96.3, <0.001	
Country							
China	5	0.64(0.52-0.76)	96.6, <0.001	0.42	0.57(0.42-0.72)	96.9, <0.001	0.41
Non-China	1	0.46(0.15-0.76)	NR		0.71(0.41-1.00)	NR	
Sample size							
≤298	3	0.65(0.48-0.81)	94.7, <0.001	0.43	0.67(0.49-0.85)	93.0, <0.001	0.28
>298	3	0.59(0.42-0.76)	97.7, <0.001		0.54(0.35-0.74)	97.7, <0.001	
Cut-off value							
≤410	3	0.73(0.66-0.81)	84.1, 0.002	<0.001	0.42(0.38-0.47)	54.7, 0.110	<0.001
>410	3	0.47(0.37-0.57)	90.2, <0.001		0.76(0.72-0.81)	0.0, 0.541	
Treatment							
Surgery	6	0.61(0.48-0.73)	96.2, <0.001	NR	0.60(0.45-0.73)	96.3, <0.001	NR
CRT	0	NR	NR		NR	NR	
Pathology							
SCC	5	0.64(0.52-0.76)	96.6, <0.001	0.42	0.57(0.42-0.72)	96.9, <0.001	0.41
Mixed	1	0.46(0.15-0.76)	NR		0.71(0.41-1.00)	NR	
Clinical stage							
0-III	5	0.61(0.47-0.74)	96.9, <0.001	0.88	0.54(0.40-0.68)	95.9, <0.001	0.10
0-IV	1	0.60(0.30-0.91)	NR		0.78(0.56-1.00)	NR	
Follow-up							
≤36	2	0.66(0.61-0.70)	53.0, 0.145	0.07	0.57(0.52-0.62)	97.6, <0.001	0.94
>36	2	0.57(0.54-0.61)	98.7, <0.001		0.52(0.48-0.56)	98.8, <0.001	
NR	2	0.71(0.65-0.76)	97.0, <0.001		0.55(0.46-0.63)	90.0, 0.002	
Age							
≤63.0	3	0.59(0.42-0.76)	97.7, <0.001	0.93	0.54(0.35-0.74)	97.7, <0.001	0.67
>63.0	2	0.55(0.48-0.62)	77.6, 0.035		0.76(0.70-0.82)	17.4, 0.271	
NR	1	NR	NR		NR	NR	
Sex ratio							
≤4.55	3	0.59(0.42-0.76)	97.7, <0.001	0.93	0.54(0.35-0.74)	97.7, <0.001	0.67
>4.55	3	0.65(0.48-0.81)	94.7, <0.001		0.67(0.49-0.85)	93.0, <0.001	
PNI							
Overall	7	0.51(0.41-0.61)	95.6, <0.001		0.67(0.56-0.77)	95.0, <0.001	
Country							
China	5	0.52(0.40-0.64)	97.0, <0.001	0.82	0.63(0.51-0.76)	95.8, <0.001	0.09
Non-China	2	0.48(0.29-0.68)	0.0, 0.412		0.76(0.60-0.91)	40.1, 0.196	
Sample size							
≤255	2	0.51(0.31-0.71)	54.7, 0.137	0.99	0.72(0.53-0.91)	0.0, 0.612	0.30
>255	5	0.51(0.39-0.63)	97.0, <0.001		0.66(0.53-0.79)	96.4, <0.001	
Cut-off value							
≤46	2	0.44(0.26-0.62)	75.3, 0.044	0.51	0.80(0.67-0.93)	0.0, 0.963	0.01

>46	5	0.53(0.42-0.65)	96.5, <0.001		0.62(0.50-0.73)	95.4, <0.001	
Treatment							
Surgery	5	0.54(0.44-0.65)	94.2, <0.001	0.30	0.65(0.52-0.78)	95.3, <0.001	0.22
Mixed	1	NR	NR		NR	NR	
NR	1	NR	NR		NR	NR	
Pathology							
SCC	5	0.52(0.40-0.64)	97.0, <0.001	0.82	0.63(0.51-0.76)	95.8, <0.001	0.09
Mixed	2	0.48(0.29-0.68)	0.0, 0.412		0.76(0.60-0.91)	40.1, 0.196	
Clinical stage							
0-III	4	0.58(0.47-0.68)	94.8, <0.001	0.17	0.60(0.47-0.73)	93.7, <0.001	0.01
0-IV	3	0.41(0.29-0.53)	84.8, 0.001		0.76(0.65-0.87)	5.0, 0.349	
Follow-up							
≤36	5	0.48(0.36-0.60)	96.1, <0.001	0.64	0.69(0.57-0.82)	94.3, <0.001	0.30
>36	2	0.57(0.39-0.75)	89.2, 0.002		0.62(0.42-0.83)	97.4, <0.001	
Age							
≤63.4	3	0.51(0.35-0.67)	98.2, <0.001	0.88	0.75(0.62-0.88)	97.1, <0.001	0.99
>63.4	2	0.48(0.41-0.55)	0.0, 0.412		0.76(0.70-0.81)	40.1, 0.196	
NR	2	0.44(0.38-0.50)	85.4, 0.009		0.79(0.71-0.86)	0.0, 0.737	
Sex ratio							
≤4.75	4	0.56(0.44-0.68)	97.2, <0.001	0.43	0.59(0.47-0.71)	96.0, <0.001	0.75
>4.75	3	0.45(0.31-0.59)	50.8, 0.131		0.77(0.67-0.88)	11.6, 0.323	
NLR							
Overall	11	0.51(0.47-0.54)	77.1, <0.001		0.70(0.64-0.76)	79.1, <0.001	
Country							
China	8	0.51(0.47-0.55)	83.8, <0.001	0.98	0.70(0.64-0.77)	71.5, 0.001	0.04
Non-China	3	0.50(0.41-0.60)	0.0, 0.800		0.71(0.60-0.81)	91.4, <0.001	
Sample size							
≤297	6	0.56(0.50-0.61)	0.0, 0.462	0.14	0.70(0.62-0.78)	78.8, <0.001	0.03
>297	5	0.48(0.43-0.53)	88.5, <0.001		0.72(0.64-0.79)	83.6, <0.001	
Cut-off value							
≤2.5	3	0.47(0.42-0.53)	33.5, 0.223	0.76	0.75(0.70-0.80)	65.6, 0.055	0.06
>2.5	7	0.51(0.46-0.55)	84.2, <0.001		0.71(0.64-0.78)	75.8, <0.001	
NR	1	NR	NR		NR	NR	
Treatment							
Surgery	7	0.48(0.43-0.52)	0.0, 0.619	0.31	0.71(0.63-0.78)	75.8, <0.001	0.05
Mixed	4	0.53(0.48-0.58)	89.3, <0.001		0.71(0.61-0.81)	85.8, 0.001	
Pathology							
SCC	8	0.51(0.47-0.55)	83.8, <0.001	0.98	0.70(0.64-0.77)	71.5, 0.001	0.04
Mixed	3	0.50(0.41-0.60)	0.0, 0.800		0.71(0.60-0.81)	91.4, <0.001	
Clinical stage							
0-III	6	0.54(0.50-0.58)	55.0, 0.049	0.14	0.70(0.62-0.78)	78.8, <0.001	0.02
0-IV	5	0.46(0.42-0.50)	0.0, 0.642		0.71(0.63-0.79)	83.6, <0.001	
Follow-up							
≤37	4	0.47(0.44-0.51)	65.3, 0.034	NR	0.68(0.61-0.73)	86.9, <0.001	NR

>37	2	0.44(0.38-0.52)	0.0, 0.497		0.76(0.71-0.81)	76.6, 0.039	
NR	5	0.54(0.52-0.57)	80.7, <0.001		0.68(0.65-0.72)	70.5, 0.009	
Age							
≤61.1	4	0.47(0.43-0.51)	37.4, 0.187	0.92	0.72(0.68-0.76)	0.0, 0.861	0.07
>61.1	6	0.53(0.47-0.59)	70.9, 0.004		0.73(0.66-0.80)	84.6, <0.001	
NR	1	NR	NR		NR	NR	
Sex ratio							
≤5.12	5	0.50(0.44-0.55)	78.3, 0.001	0.91	0.70(0.62-0.78)	83.1, <0.001	0.03
>5.12	6	0.51(0.46-0.56)	53.3, 0.058		0.71(0.63-0.78)	79.3, <0.001	
CAR							
Overall	6	0.50(0.38-0.62)	94.8, <0.001		0.84(0.71-0.91)	89.2, <0.001	
Country							
China	4	0.45(0.32-0.59)	95.9, <0.001	0.31	0.87(0.81-0.94)	90.1, <0.001	0.64
Non-China	2	0.60(0.41-0.80)	81.0, 0.022		0.68(0.51-0.85)	38.4, 0.203	
Sample size							
≤283	4	0.60(0.51-0.69)	66.7, 0.029	0.04	0.82(0.70-0.94)	86.7, <0.001	0.61
>283	2	0.33(0.23-0.43)	94.4, <0.001		0.85(0.71-0.98)	95.7, <0.001	
Cut-off value							
≤0.13	4	0.56(0.44-0.68)	87.9, <0.001	0.28	0.77(0.67-0.86)	85.4, <0.001	0.46
>0.13	2	0.37(0.21-0.53)	96.1, <0.001		0.94(0.88-1.00)	0.0, 0.665	
Treatment							
Surgery	2	0.45(0.24-0.66)	98.2, <0.001	0.71	0.85(0.72-0.98)	91.2, 0.001	0.66
Mixed	4	0.53(0.38-0.67)	81.3, 0.001		0.81(0.69-0.93)	87.8, <0.001	
Pathology							
SCC	4	0.53(0.38-0.67)	81.3, 0.001	0.65	0.81(0.69-0.93)	87.8, <0.001	0.25
Mixed	2	0.45(0.24-0.66)	98.2, <0.001		0.85(0.72-0.98)	91.2, 0.001	
Clinical stage							
0-III	3	0.46(0.29-0.63)	97.2, <0.001	0.62	0.91(0.88-0.95)	0.0, 0.814	0.22
0-IV	3	0.54(0.37-0.71)	88.1, <0.001		0.71(0.66-0.76)	29.6, 0.242	
Follow-up							
≤40	1	NR	NR	NR	NR	NR	NR
>40	1	NR	NR		NR	NR	
NR	4	0.60(0.55-0.65)	66.7, 0.029		0.80(0.74-0.85)	86.7, <0.001	
Age							
≤62.2	3	0.39(0.28-0.50)	93.8, <0.001	0.08	0.87(0.77-0.97)	92.3, <0.001	0.08
>62.2	3	0.62(0.50-0.74)	63.3, 0.066		0.78(0.63-0.92)	89.5, <0.001	
Sex ratio							
≤5.5	4	0.56(0.44-0.68)	87.9, <0.001	0.28	0.77(0.67-0.86)	85.4, <0.001	0.46
>5.5	2	0.37(0.21-0.53)	96.1, <0.001		0.94(0.88-1.00)	0.0, 0.665	
PLR							
Overall	11	0.53(0.47-0.59)	88.6, <0.001		0.65(0.60-0.70)	78.9, <0.001	
Country							
China	9	0.50(0.45-0.56)	87.5, <0.001	0.02	0.68(0.64-0.72)	78.8, <0.001	0.64
Non-China	2	0.67(0.55-0.78)	74.5, 0.048		0.52(0.39-0.64)	0.0, 0.331	

Sample size							
≤303	4	0.62(0.54-0.70)	61.2, 0.052	0.02	0.58(0.49-0.68)	37.6, 0.186	0.44
>303	7	0.49(0.43-0.54)	89.5, <0.001		0.68(0.64-0.73)	84.0, <0.001	
Cut-off value							
≤143	5	0.48(0.41-0.56)	93.1, <0.001	0.54	0.62(0.55-0.69)	87.4, <0.001	0.16
>143	5	0.57(0.53-0.60)	28.3, 0.233		0.70(0.66-0.73)	55.1, 0.064	
NR	1	NR	NR		NR	NR	
Treatment							
Surgery	9	0.52(0.46-0.59)	90.4, <0.001	0.44	0.66(0.60-0.71)	83.1, <0.001	0.20
Mixed	2	0.57(0.43-0.71)	0.0, 0.875		0.65(0.52-0.79)	0.0, 0.808	
Pathology							
SCC	10	0.51(0.46-0.56)	86.7, <0.001	0.01	0.67(0.63-0.71)	77.4, <0.001	0.31
Mixed	1	0.73(0.59-0.88)	NR		0.47(0.29-0.65)	NR	
Clinical stage							
0-III	10	0.51(0.46-0.56)	86.7, <0.001	0.01	0.67(0.63-0.71)	77.4, <0.001	0.31
0-IV	1	0.73(0.59-0.88)	NR		0.47(0.29-0.65)	NR	
Follow-up							
≤39	4	0.47(0.45-0.50)	86.9, <0.001	NR	0.62(0.59-0.66)	84.7, <0.001	NR
>39	3	0.47(0.43-0.52)	92.0, <0.001		0.71(0.67-0.76)	73.0, 0.025	
NR	4	0.58(0.55-0.62)	80.1, 0.002		0.66(0.62-0.71)	71.9, 0.014	
Age							
≤61.2	7	0.49(0.43-0.56)	89.8, <0.001	0.58	0.68(0.63-0.73)	83.6, <0.001	<0.001
>61.2	3	0.62(0.57-0.67)	71.0, 0.032		0.58(0.50-0.65)	49.8, 0.137	
NR	1	NR	NR		NR	NR	
Sex ratio							
≤4.55	5	0.46(0.39-0.52)	90.0, <0.001	0.20	0.65(0.58-0.72)	84.5, <0.001	0.04
>4.55	6	0.60(0.53-0.66)	67.9, 0.008		0.67(0.60-0.74)	73.3, 0.002	
GPS							
Overall	6	0.48(0.43-0.54)	44.1, 0.111		0.79(0.72-0.85)	20.0, 0.282	
Country							
China	2	0.51(0.44-0.58)	0.0, 0.372	0.51	0.75(0.67-0.82)	0.0, 0.920	<0.001
Non-China	4	0.47(0.39-0.54)	62.6, 0.045		0.83(0.75-0.90)	23.9, 0.268	
Sample size							
≤237	3	0.41(0.34-0.49)	0.0, 0.663	0.03	0.86(0.78-0.94)	0.0, 0.464	<0.001
>237	3	0.52(0.49-0.56)	0.0, 0.486		0.75(0.70-0.80)	0.0, 0.918	
Cut-off value							
1-2 VS 0	3	0.47(0.39-0.54)	62.0, 0.072	0.51	0.81(0.73-0.89)	59.8, 0.083	<0.001
2 VS 0	3	0.50(0.44-0.57)	35.4, 0.213		0.77(0.69-0.85)	0.0, 0.651	
Treatment							
Surgery	6	0.48(0.43-0.54)	44.1, 0.111	NR	0.79(0.72-0.85)	20.0, 0.282	NR
Mixed	0	NR	NR		NR	NR	
Pathology							
SCC	2	0.51(0.46-0.56)	0.0, 0.372	0.94	0.75(0.68-0.80)	0.0, 0.920	0.01
Mixed	3	0.48(0.40-0.55)	48.8, 0.142		0.79(0.71-0.86)	0.0, 0.714	

NR	1	NR	NR		NR	NR	
Clinical stage							
0-III	4	0.47(0.41-0.54)	43.1, 0.153	0.78	0.79(0.72-0.86)	47.3, 0.127	0.05
0-IV	2	0.51(0.42-0.60)	56.9, 0.128		0.80(0.69-0.91)	0.0, 0.458	
Follow-up							
≤40	1	NR	NR	NR	NR	NR	NR
>40	1	NR	NR		NR	NR	
NR	4	0.50(0.46-0.54)	56.5, 0.076		0.78(0.73-0.83)	41.7, 0.161	
Age							
≤62.1	1	NR	NR		NR	NR	
>62.1	3	0.51(0.47-0.56)	48.8, 0.142	0.65	0.78(0.70-0.85)	0.0, 0.714	0.01
NR	2	0.47(0.37-0.57)	61.2, 0.108		0.81(0.72-0.90)	79.6, 0.027	
Sex ratio							
≤5.48	2	0.51(0.42-0.60)	56.9, 0.128	0.78	0.80(0.69-0.91)	0.0, 0.458	0.05
>5.48	4	0.47(0.41-0.54)	43.1, 0.153		0.79(0.72-0.86)	47.3, 0.127	
LMR							
Overall	7	0.54(0.48-0.61)	84.9, <0.001		0.60(0.54-0.65)	73.5, 0.001	
Country							
China	6	0.53(0.47-0.59)	85.8, <0.001	0.20	0.60(0.55-0.66)	77.4, 0.001	0.94
Non-China	1	0.63(0.47-0.79)	NR		0.55(0.37-0.72)	NR	
Sample size							
≤280	3	0.61(0.53-0.69)	0.0, 0.832	0.04	0.56(0.47-0.65)	49.7, 0.137	0.61
>280	4	0.50(0.44-0.56)	88.8, <0.001		0.62(0.56-0.68)	82.3, 0.001	
Cut-off value							
≤3.57	4	0.56(0.48-0.64)	76.3, 0.006	0.40	0.58(0.52-0.64)	75.8, 0.006	0.38
>3.57	3	0.52(0.42-0.62)	91.2, <0.001		0.63(0.55-0.72)	40.0, 0.189	
Treatment							
Surgery	4	0.51(0.44-0.58)	88.2, <0.001	0.11	0.63(0.57-0.69)	78.0, 0.003	0.53
Mixed	3	0.59(0.51-0.67)	0.0, 0.740		0.56(0.48-0.63)	49.6, 0.137	
Pathology							
SCC	7	0.54(0.48-0.61)	84.9, <0.001	NR	0.60(0.54-0.65)	73.5, 0.001	NR
Mixed	0	NR	NR		NR	NR	
Clinical stage							
0-III	7	0.54(0.48-0.61)	84.9, <0.001	NR	0.60(0.54-0.65)	73.5, 0.001	NR
0-IV	0	NR	NR		NR	NR	
Follow-up							
≤39	2	0.52(0.41-0.64)	74.1, 0.050	0.93	0.59(0.48-0.69)	38.1, 0.204	0.34
>39	4	0.52(0.48-0.56)	90.3, <0.001		0.64(0.59-0.68)	79.3, 0.002	
NR	1	NR	NR		NR	NR	
Age							
≤61.5	4	0.50(0.44-0.56)	88.8, <0.001	0.68	0.62(0.56-0.68)	82.3, 0.001	0.06
>61.5	2	0.61(0.53-0.67)	0.0, 0.554		0.60(0.51-0.70)	26.0, 0.245	
NR	1	NR	NR		NR	NR	
Sex ratio							

≤4.32	4	0.50(0.43-0.57)	87.4, <0.001	0.74	0.59(0.51-0.66)	77.3, 0.004	0.29
>4.32	3	0.59(0.51-0.67)	0.0, 0.643		0.60(0.51-0.68)	78.6, 0.009	
mGPS							
Overall	5	0.46(0.30-0.62)	96.0, <0.001		0.80(0.72-0.86)	76.2, 0.002	
Country							
China	3	0.51(0.31-0.71)	97.8, <0.001	0.44	0.76(0.65-0.87)	86.4, 0.001	0.01
Non-China	2	0.39(0.15-0.62)	68.5, 0.075		0.84(0.76-0.93)	42.6, 0.187	
Sample size							
≤212	2	0.66(0.56-0.76)	0.0, 0.320	0.00	0.68(0.57-0.80)	78.3, 0.032	0.43
>212	3	0.32(0.24-0.41)	86.2, 0.001		0.85(0.82-0.89)	10.1, 0.329	
Cut-off value							
1-2 VS 0	4	0.42(0.26-0.58)	95.6, <0.001	0.31	0.84(0.80-0.89)	0.0, 0.503	<0.001
2 VS 0	1	0.64(0.34-0.94)	NR		0.62(0.47-0.77)	NR	
Treatment							
Surgery	3	0.32(0.24-0.41)	86.2, 0.001	0.00	0.85(0.82-0.89)	10.1, 0.329	0.43
Mixed	2	0.66(0.56-0.76)	0.0, 0.320		0.68(0.57-0.80)	78.3, 0.032	
Pathology							
SCC	4	0.50(0.32-0.67)	96.8, <0.001	0.37	0.78(0.70-0.86)	79.6, 0.002	0.01
Mixed	1	0.33(0.02-0.63)	NR		0.87(0.78-0.97)	NR	
Clinical stage							
0-III	4	0.42(0.26-0.58)	95.6, <0.001	0.28	0.84(0.80-0.89)	0.0, 0.503	0.75
0-IV	1	0.64(0.34-0.94)	NR		0.62(0.47-0.77)	NR	
Follow-up							
≤39	3	0.47(0.25-0.68)	92.3, <0.001	0.99	0.79(0.71-0.88)	84.9, 0.001	0.15
>39	1	NR	NR		NR	NR	
NR	1	NR	NR		NR	NR	
Age							
≤61.7	3	0.51(0.31-0.71)	97.8, <0.001	0.59	0.76(0.65-0.87)	86.4, 0.001	0.38
>61.7	2	0.39(0.15-0.62)	68.5, 0.075		0.84(0.76-0.93)	42.6, 0.187	
Sex ratio							
≤4.91	2	0.42(0.17-0.67)	98.4, <0.001	0.67	0.77(0.64-0.90)	93.0, <0.001	0.35
>4.91	3	0.49(0.28-0.70)	93.5, <0.001		0.82(0.73-0.91)	0.0, 0.376	

Abbreviations: OS, overall survival; CSS, cancer-specific survival; DFS, disease-free survival; EC, esophageal carcinoma; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; CAR, c-reactive protein-to-albumin ratio; SII, systemic inflammation index; PNI, prognostic nutritional index; GPS, Glasgow Prognostic Score; mGPS, modified Glasgow Prognostic Score; Ref, reference; P-reg, the P-value of meta regression; NR, not reported.

Table 1. Pair-wise comparisons between modalities for sensitivity, specificity, P-LR, N-LR, DOR and AUC.

Category	Sensitivity	*P*	Specificity	*P*	P-LR	*P*	N-LR	*P*	DOR	*P*	AUC	*P*
NLR	0.51 [0.47, 0.54]	NA	0.70 [0.64, 0.76]	NA	1.7 [1.5, 2.0]	NA	0.70 [0.66, 0.74]	NA	2.42 [1.96, 2.99]	NA	0.60 [0.56 - 0.64]	NA
PLR	0.53 [0.47, 0.59]	NA	0.65 [0.60, 0.70]	NA	1.5 [1.3, 1.8]	NA	0.72 [0.64, 0.80]	NA	2.12 [1.65, 2.73]	NA	0.63 [0.59 - 0.67]	NA
LMR	0.54 [0.48, 0.61]	NA	0.60 [0.54, 0.65]	NA	1.3 [1.2, 1.6]	NA	0.76 [0.67, 0.87]	NA	1.76 [1.34, 2.32]	NA	0.60 [0.55 - 0.64]	NA
SII	0.61 [0.48, 0.73]	NA	0.60 [0.45, 0.73]	NA	1.5 [1.2, 1.9]	NA	0.65 [0.53, 0.79]	NA	2.33 [1.61, 3.36]	NA	0.64 [0.60 - 0.68]	NA
PNI	0.51 [0.41, 0.61]	NA	0.67 [0.56, 0.77]	NA	1.6 [1.3, 1.9]	NA	0.73 [0.66, 0.81]	NA	2.14 [1.67, 2.73]	NA	0.61 [0.57 - 0.66]	NA
CAR	0.50 [0.38, 0.62]	NA	0.84 [0.71, 0.91]	NA	3.0 [1.7, 5.6]	NA	0.60 [0.46, 0.77]	NA	4.59 [2.17, 9.72]	NA	0.72 [0.68 - 0.75]	NA
GPS	0.48 [0.43, 0.54]	NA	0.79 [0.72, 0.85]	NA	2.3 [1.8, 3.0]	NA	0.65 [0.59, 0.72]	NA	3.41 [2.58, 4.51]	NA	0.67 [0.63 - 0.71]	NA
mGPS	0.46 [0.30, 0.62]	NA	0.80 [0.72, 0.86]	NA	2.3 [1.8, 2.9]	NA	0.68 [0.53, 0.86]	NA	3.18 [2.05, 4.94]	NA	0.75 [0.71 - 0.78]	NA
CAR vs GPS	50% vs 48%	＞0.05	84% vs 79%	＞0.05	3.0 vs 2.3	＞0.05	0.60 vs 0.65	＞0.05	4.59 vs 3.41	＞0.05	**0.72 vs 0.67**	**0.0327**
mGPS vs GPS	6% vs 448%	＞0.05	80% vs 79%	＞0.05	2.3 vs 2.3	＞0.05	0.68 vs 0.65	＞0.05	3.18 vs 3.41	＞0.05	**0.75 vs 0.67**	**0.0016**
CAR vs mGPS	50% vs 46%	＞0.05	84% vs 80%	＞0.05	3.0 vs 2.3	＞0.05	0.60 vs 0.68	＞0.05	4.59 vs 3.18	＞0.05	0.72 vs 0.75	＞0.05

P-DR, The pooled positive likelihood ratio; N-DR, negative likelihood ratio, DOR, diagnostic odds ratio.

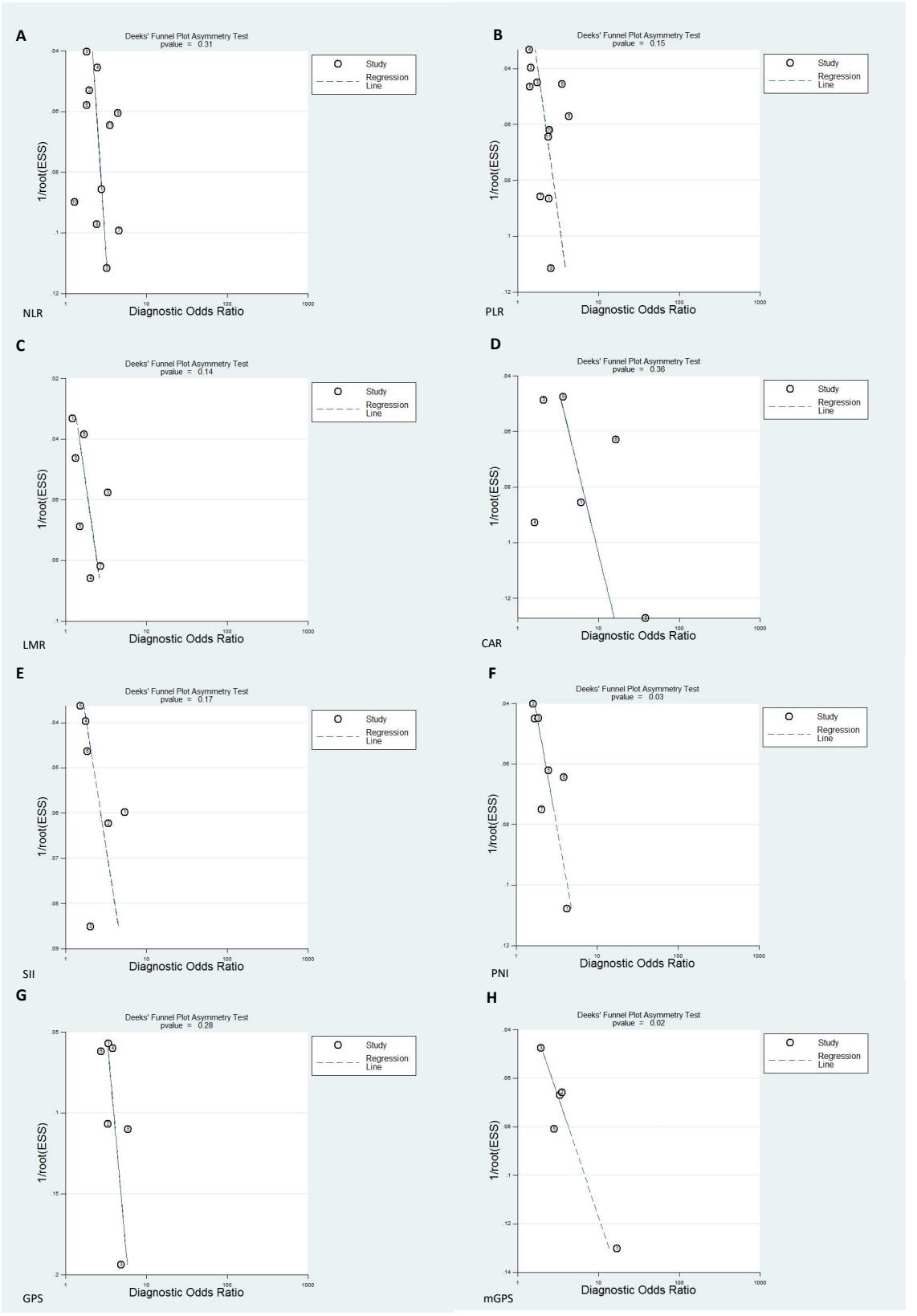

Figure 1. Deek's Funnel evaluating publication bias of DOR of 8 indicators. (A) NLR; (B) PLR; (C) LMR; (D) CAR; (E) SII; (F) PNI; (G) GPS; (H) mGPS.