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Evaluation of multiple biological indicators for combined diagnosis of gastric cancer

A retrospective analysis

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Abstract

To assess carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), platelet distribution width (PDW), neutrophil-to-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR) for gastric cancer's (GC) diagnostic efficiency, and the use of receiver operating characteristic curves (ROC) combined with logistic regression to evaluate multi-index combination's diagnostic value of GC. 773 GC patients' clinical data were retrospectively collected in the Weihai Municipal Hospital, affiliated hospital of Shandong University from April 2018 to May 2021, and selected 2368 healthy physical examination patients during the same period as the control group. A total of 3141 samples was included in this study, including 773 cases in the GC group and 2368 cases in the healthy physical examination group. The results of the overall comparison between groups showed that apart from gender, the age differences, CEA, CA19-9, PDW, NLR, and PLR were statistically significant ($P < .001$). Spearman ranks correlation analysis's results showed that CA19-9, CEA, PLR, and NLR were correlated with GC patients' clinical-stage positively, and the correlation coefficients r was 0.249, 0.280, 0.252, 0.262 (all $P < .001$), and PDW was correlated with the clinical stage negatively ($r = –0.186$, $P < .001$). The ROC curve analysis results of CEA, CA19-9, PDW, NLR and PLR showed that CEA's diagnostic cutoff value for GC was 3.175 (area under the curve [AUC] = 0.631, 95% CI: 0.606–0.655, $P < .001$), the CA19-9's diagnostic cutoff value is 19.640 (AUC = 0.589, 95% CI: 0.563–0.615, $P < .001$), PDW's diagnostic cutoff value is 15.750 (AUC = 0.799, 95% CI: 0.778–0.820, $P < .001$), NLR's diagnostic cutoff value was 2.162 (AUC = 0.699, 95% CI: 0.675–0.721, $P < .001$), and PLR's diagnostic cutoff value was 149.540 (AUC = 0.709, 95% CI: 0.688–0.732, $P < .001$). The area under the ROC curve for the combined diagnosis of GC with 5 indicators was 0.877 (95% CI: 0.860–0.894, $P < .001$), which was better than a single indicator ($P < .05$). The diagnostic efficiency of combined detection of CEA, CA19-9, PDW, NLR, and PLR is better than that of single index detection alone, which can reduce the misdiagnosis rate of GC effectively.

Abbreviations: AUC = area under the curve, BMI = body mass index, CA19-9 = carbohydrate antigen 19-9, CEA = carcinoembryonic antigen, GC = gastric cancer, NLR = neutrophil-to-lymphocyte ratio, OS = overall survival rate, PDW = platelet distribution width, PET-CT = positron emission tomography computedtomography, PLR = platelet-lymphocyte ratio, ROC = receiver operating characteristic curves.

Keywords: carcinoembryonic antigen, combined diagnosis, correlation analysis, gastric carcinoma, receiver operating characteristic curve

1. Introduction

Gastric carcinoma (GC) is 1 of the most common malignant tumors in the world. It occurs in some East Asian regions such as China mostly, but the incidence of GC in the United States is very low.[1] In China, GC ranked the third highest incidence and the second all malignant tumors' highest death rates, which has caused great damages to public health.[2] The exact cause of GC is not clear, and it may be related to eating habits, Helicobacter pylori infection, chronic gastric diseases

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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such as chronic atrophic gastritis, remnant stomach after subtotal gastrectomy, gastric polyps, genetic factors, and other factors.[3,4]

As the disease progresses, most patients with GC have no obvious early symptoms and are already in the late stage when they are discovered. The mortality rate of GC, therefore, is relatively high, and the overall survival rate (OS) is very low. Studies have shown that the early diagnosis rate of GC is low, which affects the prognosis of GC patients seriously.[5] It, therefore, is very important to improve the early detection rate of GC, and it has become a topic of high clinical concern.

At present, the commonly used examination methods of GC include computed tomography, fiber gastroscope, positron emission tomography computedtomography (PET-CT), etc., the first 2 especially are the most widely used, but there are certain limitations.[6] Although computed tomography examination is accepted by most patients because of its low pain, it can locate the stomach's space-occupying lesions only and cannot perform the pathological biopsy. Gastroscopy is the most effective method of diagnosing GC, but it is an invasive examination, which is difficult to tolerate in some patients due to fear. This examination may damage the gastric mucosa and cause congestion and edema in the throat, and the price is relatively high. Positron emission tomography can help to determine the distant metastasis and lymph nodes of GC while diagnosing GC. It has the advantages of high sensitivity and noninvasive, but its price is more expensive.[7] It, therefore, is necessary for us to try to find a new method of GC diagnosis to improve the detection rate of GC while having the advantages of noninvasive, simple and easy to obtain, less economic and painful burden.

Carcinoembryonic antigen (CEA) is a broad-spectrum tumor marker that used in gastrointestinal tumors' early diagnosis. Researchers later found that it was expressed in some malignant tumors such as breast cancer and lung cancer. It is not a specific marker for gastrointestinal tumors.[8] Carbohydrate antigen 19-9 (CA19-9) is a commonly used effective tumor marker for hepatobiliary tumors and pancreatic cancer and is also related to the occurrence of colorectal cancer, breast cancer, GC, and other tumors.[9] Platelet distribution width (PDW) is a parameter of platelet volume variation in the blood. The larger the PDW, the greater the difference in platelet size. Platelets participate in the tumor microenvironment's formation and are closely related to the development and occurrence of tumors.[10] Related studies have shown that PDW is correlated with nasopharyngeal carcinoma, breast cancer, GC, and other malignant tumors highly. In recent years, the correlation between inflammatory indicators and tumor diagnosis and prognosis has become a research hotspot. Several studies have shown that platelet-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) are prognostic and diagnostic factors for a variety of malignant tumors.[11]

Our study hopes to assess the diagnostic value of the 5 biological indicators of CEA, CA19-9, PDW, NLR, and PLR to GC by analyzing 3141 samples' clinical data from the Weihai Municipal Hospital, and to combine these indicators to improve the diagnostic efficiency of GC.

2. Patients and methods

2.1. Study design and data collection

This study is a case-control design of the diagnostic accuracy test. We collected 3141 samples' clinical data retrospectively from Weihai Municipal Hospital, from April 2018 to May 2021. Among them, 773 were in the GC group and 2368 were healthy. Inclusion criteria for the GC group: No history of surgery for gastric diseases; No acute or chronic gastroenteritis and systemic infections; No coagulation dysfunction; Pathological gold standard diagnosed as GC for the first time, not accepted other treatments; complete clinicopathological data; no liver and kidney dysfunction; no other tumors. This study was carried out with the approval of the Weihai Municipal Hospital Ethics Committee. All patient's information continued to be anonymous, and the requirement for informed consent was waived due to the study's observational nature.

We first evaluate the diagnostic value of the 5 indicators CEA, CA19-9, PDW, NLR, and PLR in the overall sample and subgroups (early GC) for GC, and then analyze the correlation between each indicator and GC clinical analysis in the GC group. Further through the receiver operating characteristic curves (ROC) and logistic regression model to select the best indicators for joint diagnosis, and finally evaluate the joint diagnosis' accuracy.

2.2. Statistical analysis

In this study's analysis, the continuous variables are skewed by the single-sample rank test apart from body mass index (BMI), so the median (interquartile range) is used for description, and the classification data is described by n (%). The Chi-square test or Mann–Whitney *U* test was used for comparison between groups. ROC analysis evaluated the diagnostic efficacy of CEA, CA19-9, PDW, NLR, and PLR on early GC and total samples, and Spearman rank correlation analysis of correlation's degree between each index and the clinical stage of GC. The disease state was used as the dependent variable, and each index was the independent variable to establish a logistic regression model, and finally, the meaningful variables were screened to establish the final model and combined with the ROC curve to achieve a joint diagnosis. All key analyses are conducted in IBM SPSS 26.0, and data visualization is performed with R.

3. Results

3.1. Clinical baseline characteristics

A total of 3141 patients were enrolled in this study, including 773 patients in the GC group, aged 64 (57–70) years old, and 2368 patients in the healthy physical examination group, aged 54 (47–63) years old. The results of the comparison between the groups showed that the age differences, CEA, CA19-9, PDW, NLR, and PLR between the 2 groups were statistically significant ($P < .001$), while there was no difference in the gender distribution and BMI of the 2 groups ($P = .246$, $P = .407$), The GC group of patients with stage I, II, III and IV respectively. The comparison between the early GC group and the healthy physical examination group in the subgroup analysis showed that the differences in age, CEA, PDW, NLR, and PLR between the 2 groups were statistically significant ($P < .001$). The difference was statistically insignificant in the CA19-9, BMI, and gender between the 2 groups, ($P > .05$) (Tables 1 and 2).

3.2. Correlation analysis

We performed a correlation analysis on the clinical analysis of CEA, CA19-9, PDW, NLR, PLR, and GC patients. The results of Spearman rank correlation analysis (Table 3) showed that CEA, CA19-9, NLR, and PLR were related to GC patients. The clinical stage of PDW was positively correlated, and the correlation coefficients r was 0.249, 0.280, 0.252, 0.262 (all $P < .001$), and PDW was negatively correlated with the clinical stage ($r = -0.186$, $P < .001$).

3.3. The diagnostic efficacy of single index for GC

The results of the ROC curve analysis of CEA, CA19-9, PDW, NLR and PLR showed (Table 4, Fig. 1) that CEA's diagnostic cutoff value for GC was 3.175 (area under the curve [AUC] = 0.631, 95% CI: 0.606–0.655, $P < .001$), the diagnostic cutoff value of CA19-9 is 19.640 (AUC = 0.589, 95% CI:

Table 1

Comparison of baseline characteristics between overall groups.

Index	GC (n = 773)	The health (n = 2368)	*P* value
Age (year)	64 (57–70)	54 (47–63)	<.001
Sex	569 (73.6)	1692 (71.5)	.246
Male	204 (26.4)	676 (28.5)	
Female			
BMI (Kg/m^2)	25.71 ± 4.31	25.57 ± 3.35	.600
CEA (ng/ml)	2.73 (1.57–5.08)	2.04 (1.35–2.92)	<.001
CA19-9 (u/ml)	10.94 (6.27–24.14)	8.94 (5.95–13.59)	<.001
PDW (%)	15.50 (11.60–16.00)	16.10 (15.90–16.40)	<.001
NLR	2.27 (1.59–3.47)	1.64 (1.26–2.09)	<.001
PLR	150.91 (111.26–211.94)	112.78 (90.94–137.54)	<.001
Staging	8 (1.0)		
0	236 (30.5)		
I	170 (22.0)		
II	214 (27.7)		
III	145 (18.8)		
IV			

*Continuous variables are described by median (interquartile range) or mean ± standard deviation, and categorical data are described by n (%).
BMI = body mass index, CA19-9 = carbohydrate antigen 19-9, CEA = carcinoembryonic antigen, GC = gastric carcinoma, NLR = neutrophil-to-lymphocyte ratio, PDW = platelet distribution width, PLR = platelet-lymphocyte ratio.

Table 2

Comparison of baseline characteristics between subgroups.

Index	Early GC (n = 244)	The health (n = 2368)	*P* value
Age (year)	63 (57–68)	54 (47–63)	<.001
Sex	176 (72.1)	1692 (71.5)	.823
male	68 (27.9)	676 (28.5)	
female			
BMI (Kg/m^2)	25.35 ± 2.97	25.57 ± 3.35	.319
CEA (ng/ml)	9.29 (5.84–15.70)	2.04 (1.35–2.92)	<.001
CA19-9 (u/ml)	2.30 (1.48–3.49)	8.94 (5.95–13.59)	.293
PDW (%)	15.80 (12.58–16.10)	16.10 (15.90–16.40)	<.001
NLR	1.90 (1.43–2.80)	1.64 (1.26–2.09)	<.001
PLR	131.70 (98.10–173.96)	112.78 (90.94–137.54)	<.001

*Continuous variables are described by median (interquartile range) or mean ± standard deviation, and categorical data are described by n (%).
BMI = body mass index, CA19-9 = carbohydrate antigen 19-9, CEA = carcinoembryonic antigen, GC = gastric carcinoma, NLR = neutrophil-to-lymphocyte ratio, PDW = platelet distribution width, PLR = platelet-lymphocyte ratio.

Table 3

Correlation analysis results.

Index	staging (*r*)	*P* value
CEA	0.249	<.001
CA19-9	0.282	<.001
PDW	–0.186	<.001
NLR	0.252	<.001
PLR	0.262	<.001

*CEA = carcinoembryonic antigen, CA19-9 = carbohydrate antigen 19-9, PDW = platelet distribution width, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-lymphocyte ratio.

0.563–0.615, $P < .001$), and the diagnostic cutoff value of PDW is 15.750 (AUC = 0.799, 95% CI: 0.778–0.820, $P < .001$), the diagnostic cutoff value of NLR was 2.162 (AUC = 0.699, 95% CI: 0.675–0.721, $P < .001$), and the diagnostic cutoff value of PLR was 149.540 (AUC = 0.709, 95% CI: 0.688–0.732, $P < .001$). We further analyzed the diagnostic efficacy of various indicators for early GC in the subgroups, and the results showed (Table 5, Fig. 2) that CEA, PDW, NLR and PLR have diagnostic cutoff values of 2.635 for GC (AUC = 0.569, 95% CI): 0.529–0.608, $P < .001$), 15.750 (AUC = 0.731, 95% CI: 0.691–0.770, $P < .001$), 2.080 (AUC = 0.622, 95% CI: 0.583–0.662, $P < .001$), 149.540 (AUC = 0.617, 95% CI: 0.577–0.658, $P < .001$), CA19-9 has no diagnostic value for early GC (AUC = 0.520, 95% CI: 0.479–0.562, $P = .293$).

3.4. Realization of combined diagnosis

3.4.1. Establishment of logistic regression model. Taking disease status as the dependent variable, CEA, CA19-9, PDW, NLR, and PLR as independent variables, fitting a logistic regression model, in the choice of the connection function, since the disease status in the ROC data is a binary variable,

Table 4

The diagnostic efficacy of single index for GC.

Index	Sensitivity	Specificity	LR+	LR-	cutoff value	AUC	*P* value
CEA	0.431	0.796	2.112	0.715	3.175	0.631	<.001
CA19-9	0.304	0.904	3.157	0.770	19.640	0.589	<.001
PDW	0.604	0.882	5.109	0.449	15.750	0.799	<.001
NLR	0.543	0.779	2.464	0.586	2.163	0.698	<.001
PLR	0.510	0.827	2.943	0.593	149.540	0.709	<.001

*CEA = carcinoembryonic antigen, CA19-9 = carbohydrate antigen 19-9, GC = gastric cancer, PDW = platelet distribution width, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-lymphocyte ratio, LR = likelihood ratio, AUC = area under the curve.

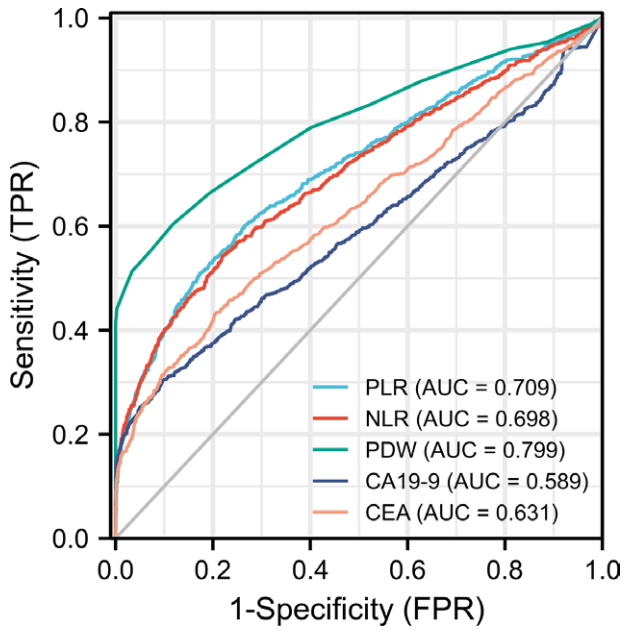

Figure 1. The diagnostic efficacy of single indicator of the overall sample. *CEA = carcinoembryonic antigen, CA19-9 = carbohydrate antigen 19-9, PDW = platelet distribution width, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-lymphocyte ratio.

the connection function can be There are many options, but usually, because the logit connection function parameter is the logarithm of the odds ratio value, it is easier to explain the meaning of the parameter changes in the model, so we choose the logit function. The final fitting results of the model are shown in (Table 6). The model equations obtained by fitting are: Model 1: logit(P) = 21.606 + 0.058 × (CEA) + 0.026 × (CA19-9) – 1.614 × (PDW))+ 0.568 × (NLR) + 0.006 × (PLR). Model 2: logit(P) = 24.537 + 0.030 × (CA19-9) – 1.761 × (PDW) + 0.765 × (NLR).

3.4.2. Realization and verification of combined diagnosis. In SPSS software, the logistic regression equation is transformed to save a list of new predictors, and the new predictors are used as indicators to be evaluated. The disease state is the gold standard, and the ROC curve is established (Figs. 3 and 4). The results showed that the area under the ROC curve for the combined diagnosis of GC with 5 indicators in the overall group was 0.877 (95% CI: 0.860–0.894, $P < .001$), and the sensitivity and specificity were 66.5% and 96.7%. The point of the largest Youden index (0.632) is further selected to determine the best cutoff value of the combined diagnosis is 0.348. The area under the ROC curve for the combined diagnosis of GC with 5 indicators in the subgroup was 0.785 (95% CI: 0.749–0.822, $P < .001$), and the sensitivity and specificity were 64.8% and 81.7%. The maximum value of the Youden index (0.464) is used to determine the best cutoff value for a combined diagnosis of 0.869. In clinical application, each index is substituted into the regression equation. The value greater than the cutoff value is abnormal, and the value less than this value is normal.

We further conducted internal verification of the combined diagnosis results between the overall and subgroups, and the results of the specific verification (see Table 7). The results of internal verification showed that the accuracy rate of joint diagnosis prediction in the overall group was 89.2%, and the accuracy rate of joint diagnosis prediction in the subgroup was 78.0%, and the prediction results were relatively ideal.

4. Discussion

Since most GC patients have no symptoms before the disease progresses to advanced stages, early diagnosis is considered to be the core issue of some important medical associations, such as Union for International Cancer Control, American Joint Committee on Cancer, and Japan Gastric Cancer Association.[12] At present, gastroscopy is the most effective method recommended in the guidelines, but this examination item will cause great pain to patients, and painless gastroscopy brings a higher economic burden, so it is difficult to apply gastroscopy to early cancer screening in Asian countries.[13] At present, the most commonly used tumor markers are CEA and CA199, but these 2 markers have poor specificity and sensitivity and can be found in other tumors, such as pancreatic cancer.

The connection between cancer and inflammation was first discovered in the 19th century, and tumor cells appeared in the context of chronic inflammation.[14] With the progress of

Table 5

The diagnostic efficacy of a single index in the subgroups for early GC.

Index	Sensitivity	Specificity	LR+	LR-	cutoff value	AUC	*P* value
CEA	0.447	0.688	1.433	0.804	2.635	0.569	.000
CA19-9	0.209	0.875	1.672	0.904	18.175	0.520	.293
PDW	0.492	0.882	4.159	0.576	15.750	0.731	.000
NLR	0.447	0.748	1.772	0.739	2.080	0.622	.000
PLR	0.393	0.827	2.272	0.734	149.540	0.617	.000

*CEA = carcinoembryonic antigen, CA19-9 = carbohydrate antigen 19-9, GC = gastric cancer, PDW = platelet distribution width,NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-lymphocyte ratio, LR = likelihood ratio, AUC = area under the curve.

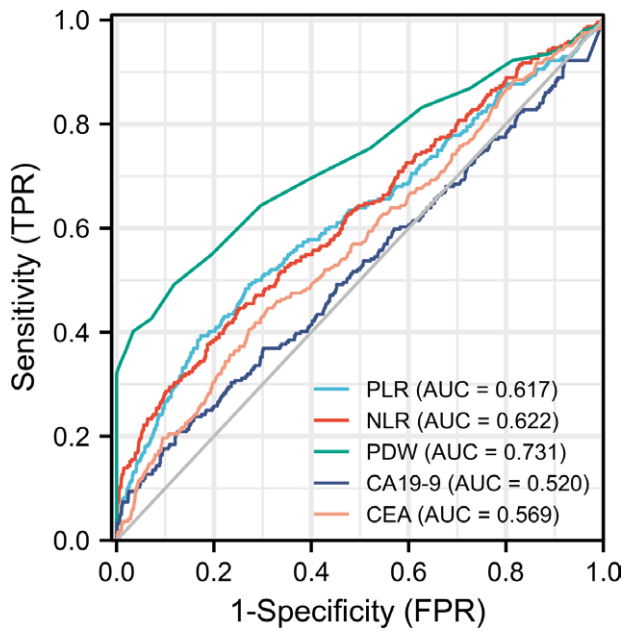

Figure 2. Diagnostic efficacy of single index in subgroups. *CEA = carcinoembryonic antigen, CA19-9 = carbohydrate antigen 19-9, PDW = platelet distribution width,NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-lymphocyte ratio.

research, some scholars have found that the progress of cancer will be accompanied by systemic inflammation, which provides new ideas for the diagnosis of early GC.[15] Pathologists often observe "cancer-related inflammation" on pathological slices of GC, once again proving that there is theoretical support for inflammation and cancer. The abnormal phenotype of the tumor itself may stimulate the chemotaxis of inflammatory leukocytes to the cancer tissue. In addition, the physical and chemical infiltration, invasion, and destruction of the surrounding tissues by the tumor can also cause nonspecific inflammatory reactions.[16] Recently, it has been reported in the literature that circulating tumor cells enter the peripheral blood to trigger an immune response, including an increase in the proportion of cancer-related macrophages and neutrophils. This relationship between systemic inflammation and tumors has always been of interest to researchers. NLR and PLR are markers of systemic inflammation, which contribute to the early diagnosis of GC.

The current research mainly focuses on the diagnosis of early GC by PLR and NLR, the prediction of GC lymph node metastasis, and the diagnosis of high-grade GC. Although PLR and NLR have certain diagnostic capabilities for GC, their sensitivity and specificity are poor.[17] This study combined CEA, CA19-9, PDW, and other previously proven tumor markers for joint diagnosis, to evaluate the diagnostic efficacy of joint diagnosis, to increase the ability of tumor markers to diagnose GC and early GC diagnosis. Neutrophils account for 50% to 70% of the total number of white blood cells in the human circulation and promote cancer cell proliferation, vascular transformation, and metastasis by producing erythrocyte angiogenesis chemokines and vascular endothelial growth factors.[18] It is currently believed that peripheral blood lymphocytes have cytotoxic effects to inhibit tumor growth.[19] In addition, platelets have also been found to be related to tumor development, involving tumor progression and metastasis. Cancer cells secrete active substances such as interleukin-6 to promote platelet production and activation. Activated platelets can also secrete vascular endothelial growth factor, platelet-derived growth factor, and transforming growth factor-β to promote angiogenesis in cancer tissues.[20,21]

We analyzed the correlation between CEA, CA19-9, PDW, NLR, PLR, and the clinical stage of GC patients. CEA, CA19-9, NLR, and PLR were positively correlated with the clinical stage of GC patients, and the correlation coefficient r was 0.249, 0.280, 0.252, 0.262 respectively (all $P < .001$). PDW was negatively correlated with the clinical stage ($r = -0.186$, $P < .001$). CEA and CA19-9 are recognized as tumor markers of gastrointestinal tumors, and it has been found in several studies that they are positively correlated with the clinical stage of GC. NLR and PLR As shown above, neutrophils and platelets promote tumor metastasis and development. Therefore, the higher the clinical stage, the higher the value of PLR and NLR.[22] Some scholars have also obtained similar results. Low preoperative PLR and NLR levels are associated with better clinicopathological characteristics, including decreased depth of invasion, decreased lymph node metastasis, and early tumor staging.[23] PLR and NLR are also related to the OS and disease-free survival rate of GC patients. The higher preoperative NLR and PLR reduce OS and disease-free survival rate. After tumor resection, PLR and NLR were significantly reduced.[24] All this supports the conclusion of this study. In addition, we found that PDW is negatively correlated with the clinical stage of GC patients, that is, the higher the PDW, the lower the tumor stage of GC patients. Studies have proved this point. Ding Huaqun and others have found that PDW is a protective factor for the prognosis of patients with GC.[25,26] There are similar results with this study, and PDW has a certain effect on GC metastasis.[27]

The ROC curve analysis results of CEA, CA19-9, PDW, NLR and PLR showed that CEA's diagnostic cutoff value for GC was 3.175 (AUC = 0.631, 95% CI: 0.606–0.655, $P < .001$), the diagnosis of CA19-9 The cutoff value is 19.640 (AUC = 0.589, 95% CI: 0.563–0.615, $P < .001$), the diagnostic cutoff value of PDW is 15.750 (AUC = 0.799, 95% CI: 0.778–0.820, $P < .001$), the diagnosis of NLR The cutoff value was 2.162 (AUC = 0.698, 95% CI: 0.675–0.721, $P < .001$), and the diagnostic cutoff value of PLR was 149.540 (AUC = 0.709, 95% CI: 0.687–0.732, $P < .001$). Zhao et al studied the diagnostic value of NLR and PLR for GC. The critical values of NLR and PLR are 2.48 and 143.39, respectively, which are similar to the results of this study.[28] In the study of stage III GC, Kambara et al found that the cutoff values of CEA and CA19-9 were

Table 6

Final fitting results of the model.

Index	Model 1				Model 2			
	Coefficients	OR	95% CI	*P* value	Coefficients	OR	95% CI	*P* value
CEA	0.058	1.060	1.025–1.097	.001	–	–	–	–
CA19-9	0.026	1.026	1.018–1.035	<.001	0.030	1.030	1.022-1.039	<.001
PDW	-1.614	0.199	0.155–0.256	<.001	-1.761	0.172	0.132-0.223	<.001
NLR	0.568	1.764	1.545–2.015	<.001	0.765	2.149	1.917-2.409	<.001
PLR	0.006	1.006	1.004–1.009	<.001	–	–	–	–

*CEA = carcinoembryonic antigen, CA19-9 = carbohydrate antigen 19-9, CI = confidence interval, OR = odds ratio, PDW = platelet distribution width, NLR = neutrophil-to-lymphocyte ratio, PLR = platelet-lymphocyte ratio.

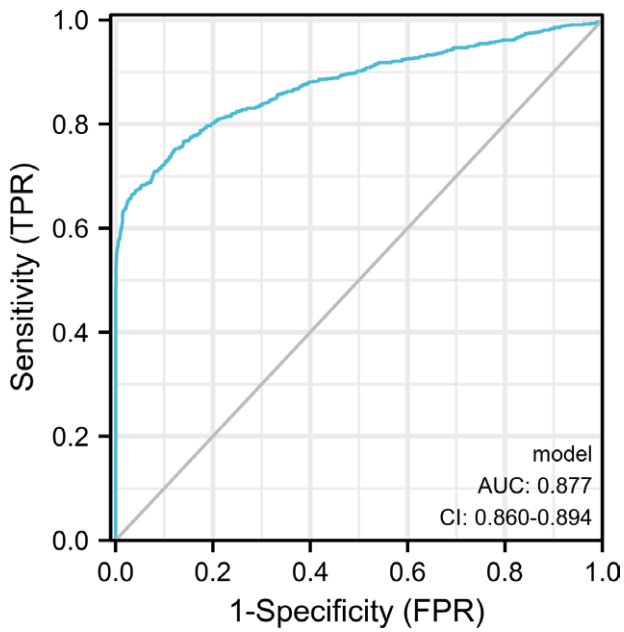

Figure 3. Combined diagnosis of the overall sample.

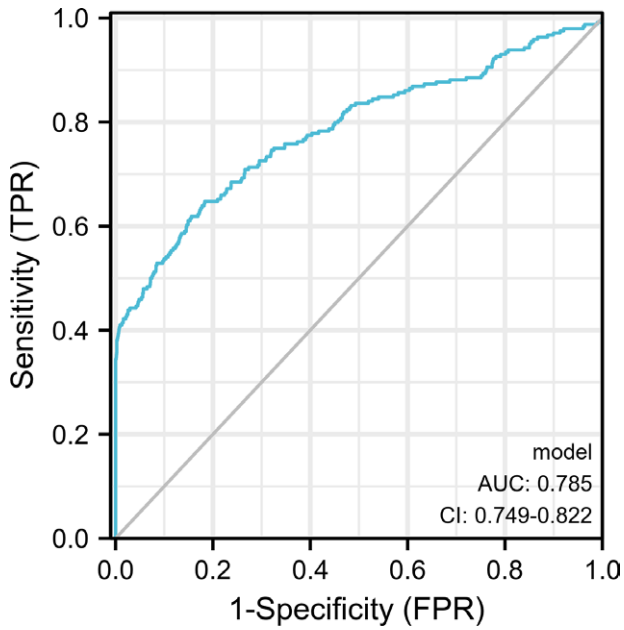

Figure 4. Combined diagnosis of subgroup.

2.9 ng/mL and 46.3 U/mL.[29] In this study, the area under the curve of PDW, NLR, and PLR was significantly higher than that of CEA and CA19-9, which was statistically significant. The systemic inflammation index was higher than the traditional tumor index. This view has also been corroborated in other studies.[11]

We found that the diagnostic value of systemic inflammation markers NLR and PLR in patients with GC is higher than that in patients with early GC. The diagnostic cutoff values of CEA, PDW, NLR and PLR for GC were 2.635 (AUC = 0.569, 95% CI: 0.529–0.608, $P < .001$), 15.750 (AUC = 0.731, 95% CI: 0.691–0.770, $P < .001$), 2.080 (AUC = 0.622, 95% CI: 0.583–0.662, $P < .001$), 149.540 (AUC = 0.617, 95% CI: 0.577–0.658, $P < .001$), CA19-9 has no diagnostic value for early GC (AUC = 0.520, 95% CI: 0.479–0.562, $P = .293$). To improve the sensitivity of GC diagnosis, we performed logistic regression analysis and used the ROC curve to determine the optimal cut-off value. The area under the ROC curve of the predictive value of ROC in the combined diagnosis of GC was 0.877 ($P < .001$), the sensitivity and specificity distributions were 66.5% and 96.7%, and the best cutoff value was 0.348. In the diagnosis of early GC, the area under the ROC curve for the combined diagnosis of 5 indicators was 0.785 (95% CI: 0.749–0.822, $P < .001$), and the sensitivity and specificity when the best cutoff value was 0.869 were 64.8% and 81.7%. The internal verification results indicate that the accuracy of combined diagnosis of GC is 89.2%, and the accuracy of combined diagnosis of early GC is 78%. Studies have combined CEA, AFP, CA125, CA19-9, and AFP to diagnose GC, with an AUC of 0.785 and an accuracy rate of 74.2%.[30]

This study also has some limitations. GC is 1 of the most widely distributed cancers in different regions. This study is a single-center data and requires further multi-center data support. In addition, the control group of this study was a healthy population, and Helicobacter pylori infection was not discussed, and patients with erosive gastritis were not included in the control group to evaluate whether the results of this study would be affected by local inflammation and infection. However, in non-inflammatory thyroid cancer and breast cancer, it has been proved that the values of NLR and PLR are related to the progression of the disease,[31,32] which indicates that the above changes may not be caused by local inflammation but maybe cancer cells entering the peripheral blood.

This study proves that CEA, CA19-9, PDW, NLR, and PLR have diagnostic value for GC. The same CEA, PDW, NLR, and PLR have diagnostic value for patients with early GC. Although our study still has a long way to go in supplementing the international guidelines for GC diagnosis and treatment, it does not prevent clinicians from using systemic inflammation markers as a method for screening and identifying high-risk groups.

5. Conclusions

CEA, CA19-9, PDW, NLR, and PLR are of limited value in the diagnosis of GC. Combined diagnosis can help improve the diagnostic efficiency of GC.

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Table 7

Overall and subgroup internal verification results.

				Prediction	
	Abnormal	Normal		Abnormal	Normal
GC	466 (14.8)	307 (9.8)	Early GC	86 (2.7)	158 (5)
The health	31 (1)	2337 (74.4)	The health	4 (0.1)	2364 (75.2)

Author contributions

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