# Comparative study of preoperative prediction scores for lymph node metastasis in gastric and colon cancer patients

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**Research**

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# Abstract

**Background:** Surgery combined with chemo-radiotherapy is a recognized model for the treatment of gastric and colon cancers. Lymph node metastasis determines the patient's surgical or comprehensive treatment plan. This analytical study aims to compare preoperative prediction scores to better predict lymph node metastasis in gastric and colon cancer patients.

**Methods:** This study comprised 768 patients, which included 312 patients with gastric cancer and 462 with colon cancer. Preoperative clinical tumor characteristics, serum markers, and immune indices were evaluated using single-factor analysis. Logistic analysis was designed to recognize independent predictors of lymph node metastasis in these patients. The independent risk factors were integrated into preoperative prediction scores, which were accurately assessed using receiver operating characteristic (ROC) curves.

**Results:** Results showed that serum markers (CA125, hemoglobin, albumin), immune indices (S100, CD31, d2–40), and tumor characteristics (pathological type, size) were independent risk factors for lymph node metastasis in patients with gastric and colon cancer. The preoperative prediction scores reliably predicted lymph node metastasis in gastric and colon cancer patients with a higher area under the ROC curve (0.901). The area was 0.923 and 0.870 in gastric cancer and colon cancer, respectively. Based on the ROC curve, the ideal cutoff value of preoperative prediction scores to predict lymph node metastasis was established to be 287.

**Conclusion:** The preoperative prediction scores is a useful indicator that can be applied to predict lymph node metastasis in gastric and colon cancer patients.


# Introduction

Gastric cancer and colon cancer are the two most common malignant tumors of the digestive tract occupying the third and second place, respectively, in cancer-related mortalities [1,2]. Surgical intervention continues to be the most effective way to treat gastric and colon cancers. However, the rate of postoperative cancer recurrence is high, and the long-term survival rate in patients is low. Lymph node metastasis is a common pattern observed in the advanced stages of cancer and a significant cause of death. More than 50% of gastric and colon cancer patients have lymph node metastases at the time of diagnosis, which results in a 5-year survival rate of less than 30% [3].

At present, surgery combined with chemo-radiotherapy is a recognized model for the treatment of some gastric and colon cancers. Lymph node metastasis is the basis for clinical tumor staging. It determines the patient's surgical or comprehensive treatment plan. The degree of metastasis is an indicator, which plays an essential role in designing an effective treatment and reducing trauma, which in turn, could considerably improve the patient's prognosis [4]. Therefore, accurate preoperative prediction of lymph node metastasis is crucial.

In recent years, with the steady development of radiographic-detection technology, new imaging diagnostic tools have gradually attracted the attention of clinicians. However, the sensitivity and specificity of techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), to scan lymph nodes with a diameter of less than 1 cm are still low [5].Thus, these diagnostic tools are often of limited use in such patients. Some studies have shown that positron-emission tomography integrated with computed tomography (PET-CT) can independently predict lymph node metastasis of gastric cancers. But the use of this technique is limited owing to its high false-positive rate and cost [6].

The study of preoperative serum indicators to predict lymph node metastases has also been widely reported. These are similar to serum tumor markers, such as CA125, CEA, and CA199, but have low sensitivity and specificity. Some researchers have tried to improve its predictive value by combining several serum tumor markers [7]. In different types of cancer treatment, the platelet to lymphocyte ratios (PLR) and neutrophil to lymphocyte ratios (NLR) are crucial independent risk factors [8]. However, the value of these preoperative serum markers in diagnosing lymph node metastasis alone is limited. With the development of tumor immunology, the relationship between the clinicopathologic features of the tumors and lymph node metastasis in gastric and colon cancer patients is gradually being recognized. Till date, few studies have reported the combination of preoperative serum markers and clinicopathologic features to predict lymph node metastasis.

Therefore, our study aimed to better predict lymph node metastasis in gastric and colon cancer patients and help improve the accuracy of preoperative diagnoses. We compared the preoperative prediction scores in patients who had undergone surgery. We found that these scores were helpful and reliable in predicting lymph node metastasis in gastric and colon cancer patients. Thus, these patients could receive personalized therapy.

# Materials And Methods

### *Patients*

This study retrospectively analyzed the data of 833 patients with gastric and colon cancers who underwent gastric and colon cancer surgery in The Dingli Clinical Institute of Wenzhou Medical University (Wenzhou Central Hospital) from January 2010 to January 2018. The following patient information was collected and recorded: basic information (age, sex, BMI), preoperative serum markers (tumor markers, routine blood index, albumin), tumor characteristics (size, location, pathological type, depth of invasion, histopathological differentiation, lymph node metastasis), and immunology indices (CD31, MRP3, EGFR, P53, CDX2). Histopathological differentiation was classified as "well-differentiated" (moderately or highly differentiated) and "poorly differentiated" (poorly differentiated or undifferentiated) tumors. The pathological types are divided into ulcer and non-ulcer types. All patients were examined by preoperative histologic examination. Exclusion criteria were as follows: (1) history of other malignancies (10 cases), (2) history of gastrointestinal resections (6 cases), (3) history of distant metastases (9 cases), (4) history of preoperative chemo-radiotherapy (15 cases), (5) history of liver diseases such as cirrhosis (8 cases),

(6) history of coagulation disorders and autoimmune diseases (11 cases), and (7) history of serious hematologic diseases (6 cases). Consequently, 768 patients were included. This study was authorized by the committee of The Dingli Clinical Institute of Wenzhou Medical University (Wenzhou Central Hospital). All patients were informed and signed informed consent was obtained from each patient.

### *Diagnosis of lymph node metastasis*

The pathological results of the preoperative endoscopic biopsy, intraoperative frozen sections and postoperative paraffin sections were used to diagnose lymph node metastasis.

### *The cutoff point of the preoperative prediction scores*

Receiver operating characteristic (ROC) curves were plotted. The cutoff point of the preoperative prediction scores were defined as the maximum value of the Youden index. Subsequently, two groups of patients were divided according to the cutoff point, for further study.

### *Statistical analysis*

Statistical software SPSS 21.0 for Windows (SPSS, Chicago, IL, USA) was used for data analysis. First, we conducted a descriptive study of the clinicopathological characteristics of the patients. Second, we compared patients in the following two groups: the lymph node metastasis group (LMPG) and non-lymph node metastasis group (LMNG). Kolmogorov-Smirnov test was used to verify the normality of AFP, CEA, neutrophil, lymphocyte, hemoglobin, and albumin levels. Normal distributed data are represented using mean and standard deviation values, while non-normal distributed data are represented using the median and interquartile range values. Gender, age, tumor size, pathological type, depth of invasion and other categorical variables are represented using frequencies and percentages. Univariate analysis of variables was performed for the two groups to determine the risk factors for lymph node metastasis. For numerical non-normal variables, Mann-Whitney U test was used, while $\chi 2$ or Fisher tests were used for categorical variables. Based on the results of the analysis, multivariate logistic regression analysis was used to determine the odds ratio (OR) and 95% confidence interval (CI) of independent risk factors. The area under the ROC curves (AUC) was used to compare the preoperative prediction scores with other independent clinicopathological features. The cut-off value of the indicator was obtained based on the ROC curve to better predict lymph node metastasis. $P<0.05$ was considered statistically significant.

## Results

### *Patient characteristics*

As shown in Table 1, among the 768 patients, 510 were male and 258 were female. The median age of the patients was 66 years, and the quartile ranged from 58 to 75 years. The average tumor size of the patients was 4.12 cm. There were 312 patients with gastric cancer and 462 with colon cancer. The majority (531 cases) were at stage T3/4. According to the pathological type, the majority (73.4%) of patients with cancers were classified as ulcerative. Based on histopathological findings, the patients had

"well-differentiated" (573) and "poorly differentiated" tumors (195). Lymph node metastasis had occurred in 384 patients (6 of whom had lost clinical data).

### *Characteristics of preoperative serum markers in gastric and colon cancer patients with lymph node metastasis*

As shown in Table 2, CA125, neutrophils, NLR, and PLR were significantly higher in LMPG than LMNG ($P<0.05$). In contrast, LMNG had higher hemoglobin levels, erythrocyte numbers, and albumin values ($P<0.05$). The ROC curve was applied to further analyze the significantly different variables. As shown in Fig 1, the AUC areas of CA125 (0.602, 95% CI 0.529–0.675) and hemoglobin (0.618, 95% CI 0.546–0.691) were larger, but their sensitivity and specificity were still low.

### *Univariate analysis of clinicopathologic characteristics*

The $\chi 2$ test was used to verify the relationship between clinicopathologic features and lymph node metastasis in gastric and colon cancer patients. As shown in Table 3, tumor size ($P=0.012$), pathological type ($P=0.000$), histopathological differentiation ($P=0.000$), depth of invasion ($P=0.000$), S100 ($P=0.000$), and CD31/ d2–40 ($P=0.000$) were significantly different in LMPG and LMNG. In contrast, there were no significant differences in the body mass index, gender, age, or BMI between the two groups. Among these parameters, S100 positive indicates nerve infiltration, while CD31/ d2–40 positive indicates vascular infiltration.

### *Multivariate analysis of lymph node metastasis*

Logistic multivariate regression analysis was used to examine independent risk factors for lymph node metastasis. As shown in Table 4, lymph node metastasis in gastric cancer patients was significantly associated with albumin (OR=7.804, $P=0.006$), histopathological differentiation (OR=3.601, $P=0.066$), depth of invasion (OR=5.982, $P=0.008$), and vascular infiltration (OR=29.251, $P=0.000$). That was significantly associated with CA125 (OR=2.660, $P=0.032$), PLR (OR=3.896, $P=0.008$), vascular infiltration (OR=9.177, $P=0.000$), and nerve infiltration (OR=8.103, $P=0.001$) in colon cancer patients. Thus, independent risk factors were different in the two groups. Integrating these two patient groups, as shown in Table 5, indicated significant association with CA125 (OR=2.851, $P=0.009$), albumin (OR=2.334, $P=0.050$), hemoglobin (OR=3.255, $P=0.008$), pathological type (OR=2.828, $P=0.021$), tumor size (OR=15.847, $P=0.015$), vascular infiltration (OR=18.200, $P=0.000$), and nerve infiltration (OR=2.812, $P=0.016$). From this data, we can derive independent risk factors for gastric and colon cancers.

### *Construction of the preoperative prediction scores for lymph node metastasis in gastric and colon cancers*

Based on multivariate logistic regression analysis, independent risk factors were selected. As shown in Table 5, the score for each independent risk factor was obtained by logarithmic conversion of its own OR value and multiplying by 100. The preoperative prediction scores were carried out by summing up each score and marking them as Score. ROC curve analysis was used to further determine whether the

preoperative prediction scores had high accuracy in predicting lymph node metastasis in gastric and colon cancers. As shown in Figure 2, the AUC value was 0.901 in gastric and colon cancer patients. Compared to other independent risk factors for gastric cancer and colon cancer, as shown in Figures 3 and 4, the AUC values were (0.923, 95% CI 0.866–0.980) and (0.870, 95% CI 0.813–0926) respectively, which were higher. Therefore, it was more reliable as a predictor of lymph node metastasis in gastric cancer and colon cancer patients.

### *The relationship between preoperative prediction scores and different clinicopathologic characteristics in gastric and colon cancer patients*

Based on the ROC curve, the cutoff value of the preoperative prediction scores for lymph node metastasis was 287. The specificity and sensitivity of this diagnosis were 88.1% and 75%, respectively. According to the cutoff value, the gastric and colon cancer patients were divided into "high Score group (≥ 287)" and "low Score group (<287)." Among the enrolled patients, the high Score group accounted for 43.7%. As shown in Table 6, according to the clinicopathological characteristics of our study, a higher score was associated with a larger tumor size, a more severe pathological cancer type, a higher degree of differentiation, a deeper degree of invasion, a higher invasion range, and a higher rate of lymph node metastasis. These findings suggested that the preoperative prediction scores was a stronger predictor of lymph node metastasis in gastric and colon cancer patients than other independent indicators. Our results also suggested that using the numerical value 287 as the cutoff point could provide more effective information.

## Discussion

Lymph node metastasis is the most common metastatic model of gastric and colon cancers. With the development of surgery in the management of these cancers, laparoscopic surgery, by virtue of its short-term minimally invasive advantages and long-term safety, has been confirmed as an early alternative for gastric and colon cancers by several clinical randomized controlled trials and meta-analyses [9,10]. However, in the case of advanced tumors, the use of laparoscopy is still controversial [11]. In addition, MAGIC, FNCLCC, and FFCD studies [12,13] report that preoperative chemotherapy can not only play a role in reducing the period, but also prolong survival. Therefore, preoperative prediction of lymph node metastasis is crucial in improving the surgical outcomes and reducing the extent of damage caused to patients.

Currently, clinical laparoscopy and pathological biopsy are the gold standards for treatment, however, the degree of trauma caused by these procedures render them less desirable. Therefore, non-invasive diagnosis models have a good scope for further exploration. CT and MRI are the most common techniques used to predict lymph node metastasis. However, their sensitivity is only 50% in the determination of metastasis of lymph nodes that are 5 mm or smaller [5]. While Pet-CT can assess the involvement of lymph nodes and distant organs in tumor patients [14], its high cost outweighs its

popularity. Therefore, effective methods are urgently needed for the preoperative prediction of lymph node metastasis in gastric and colon cancer patients.

Preoperative serum markers are commonly used in predicting lymph node metastasis of gastrointestinal tumors. In the current treatment scenario, serum tumor markers are most commonly used, but they have not been widely adopted owing to their low sensitivity and specificity. Some researchers [7] use a combination of several markers to improve the sensitivity of diagnoses (96.3%) and specificities (69.8%), however, there are only few such clinical studies that are relevant. In addition, the inflammatory response exhibited by various organ systems has received more attention during the development of tumors [15]. Chronic inflammatory response induces lymphocyte to infiltrate into the tumor, and consequently, into the surrounding tissues, thus increasing the chances of metastases. Studies have shown that PLR and NLR contribute to the diagnoses and prognoses of malignant tumors [16]. In our study, CA125 (OR=2.660, P=0.032) and PLR (OR=3.896, P=0.008) were independent risk factors for lymph node metastasis in colon cancer patients, but not in those with gastric cancer. Apparently, these variables could not be used exclusively in predicting lymph node metastasis in all patients.

With the development and use of immunohistochemistry, it is possible to predict the lymph node metastasis of tumors more accurately. Li found that the metastasis rate was higher in T4 stage gastric cancer patients, with a lower degree of differentiation, and Borrmann type  +  [17]. In addition, a study [18] found that the gross type, pathological grade, and invasion depth were closely associated with lymph node metastasis in colon cancer. These clinicopathological features can be confirmed using preoperative endoscopic examination. Therefore, we attempted to analyze the relationship between lymph node metastasis and clinicopathological features in gastric and colon cancers.

Scartozzi [19] studied 734 gastric cancer patients and revealed that a positive rate of nerve infiltration (NI) and vascular infiltration (VI) was 26%, which is related to lymph node metastasis. In our study, the values for NI and VI were 35.43% and 39.76%, respectively. We used HE and S100, D2-40, and CD31 protein immunohistochemical staining to improve the accuracy of NI and VI. The effect of VI on gastric cancer and colon cancer has been studied [20,21]. But the effect of NI presented different sounds. Although the relationship between NI and prognosis has been evaluated by meta-analysis of colon cancer studies [22], this relationship remains controversial. A meta-analysis [23] included a total of 30590 gastric cancer patients in 24 studies and revealed that the NI positive rate was 6.8–75.6%, with an average positive rate of 40.9%. The difference in NI positive rate in each study is large, which is mainly due to the difference in the definition of NI in each study. Currently, there is still no unified standard for the definition of NI. Tanaka reports [24] that NI has a prognostic value in T2 grade gastric tumor patients, but not in grade T3/4 tumor patients. Another study [25] reports that NI has no statistical significance in cardiac cancers. Our study too, found that NI was not an independent risk factor for gastric cancer.

Ren [26] reports that tumor invasion depth is an independent risk factor for lymph node metastasis in gastric cancers. A study by Bravo [27] indicates that the risk of lymph node metastasis by tumor infiltration into the submucosa is 3.103 times higher than that of the tumor confined to the mucosa. We

obtained similar results in our study, with the only difference being the type of cancer evaluated. These findings can be attributed to the abundant lymphatic vascular network in the gastric submucosa and the higher concentration of lymphatic reflux channels in the serosal layer. In addition, it is seen in Kodera's study [28] that the lymph node metastasis rate for patients with well-differentiated gastric cancer is 6.9%, whereas this value for patients with poorly-differentiated gastric cancer is 13.0%. This difference between groups is statistically significant ($P<0.05$). The relationship between the degree of differentiation and lymph node metastasis in colon cancer is still unclear, which is consistent with our study. There are few studies exploring the relationship between pathological types and lymph node metastasis. Wang [29] found no correlation between pathological types and lymph node metastasis in a study of 103 cases of early gastric cancer. In our research, we found that the pathological nature of the tumor was an independent risk factor for lymph node metastasis in gastric and colon cancer patients ($P=0.021$), however, the subdivision into gastric and colon cancer patients was not statistically significant. It is considered that the number of early cancer cases in our study is relatively small, and the determination of the type of pathology is mostly dependent on the subjective judgment of endoscopists and surgeons. In some cases, the pathological type is inconsistent with that observed after postoperative pathology, which may be attributed to the experience of clinicians and their judgment of intraoperative lesions.

Based on these differences, we attempted to identify independent risk factors for lymph node metastasis in gastric and colon cancer patients. In order to increase the accuracy of predicting lymph node metastasis preoperatively, multivariate logistic regression analyses were performed by combining serum characteristics and clinicopathological characteristics. These parameters have rarely been considered in previous studies. We determined that CA125, hemoglobin, albumin, tumor size, pathological type, nerve invasion, and vascular invasion were all independent risk factors for lymph node metastasis in gastric and colon cancers. Finally, the preoperative prediction scores, including the above independent risk factors were established. Subsequently, ROC analyses were performed to verify the diagnostic accuracy of the preoperative prediction scores. As expected, the AUC values of the indicator in lymph node metastasis of gastric and colon cancers were 0.923 and 0.870, respectively. The sensitivity of both was 92.2%, specificity was 78.9% and 60.2%, respectively, thereby significantly improving the accuracy. Therefore, we believe that the preoperative prediction scores have a strong preoperative diagnostic value for lymph node metastasis in gastric and colon cancers.

The ROC curve was used to further determine the cutoff value of Score for lymph node metastasis in gastric and colon cancers and was established to be 287. Accordingly, patients were divided into a high Score group ($\geq 287$) and a low Score group ($< 287$). Further studies revealed that Score was firmly related to several tumor characteristics. A higher Score was related to a larger tumor size, a certain pathological type, increased differentiation, a deeper degree of invasion, and a more severe lymph node metastasis. Thus, we believe that the cutoff value of 287 for Score is ideal for the preoperative prediction of lymph node metastasis in gastric and colon cancers. This preoperative score includes serum indicators and clinicopathological features to make it more comprehensive and accurate. In addition, all involved indicators can be confirmed by preoperative blood tests and preoperative endoscopic examination, which are convenient, inexpensive, and suitable for all patients. Combined with clinical practicality and

accuracy, the preoperative score can be used as a reliable indicator for the development of preoperative surgical plans and comprehensive treatment regimens.

There are some limitations in our study that cannot be ignored.As this was a retrospective study, some data can be accurately obtained after surgery, including infiltration depth, lymphatic infiltration, and pathological type. In addition, the prognostic analysis of patients was not included in our study. Moreover, data of all patients were obtained from one hospital. Most importantly, our model can only be used as an auxiliary tool. It still needs to be validated by extensive multicenter prospective studies.

# Conclusion

This is the first study of its kind to explore the relationship between the preoperative prediction scores and lymph node metastasis in gastric and colon cancers. We discovered that the preoperative prediction scores were independently associated with lymph node metastasis, which significantly improved diagnostic accuracy and could be used to predict lymph node metastases, so as to personalize individual treatments. Additionally, this method is an economical and a convenient tool for predicting lymph node metastasis.

# Declarations


### Acknowledgments

Not applicable


### Author Contributions

X.S conceived and designed the study. M.L and CM.L were responsible for sample collection. XJ.Z and XD.C performed the experiments. M.L and XD.C analyzed and interpreted the data. XJ.Z wrote the manuscript and X.S revised the manuscript. All authors discussed the results and implications of the study.


### Funding

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### Availability of data and materials

Not applicable

### Ethics approval and consent to participate

The study was approved by the Hospital Ethics Committee

### Consent for publication

Not applicable

### Competing interests

The authors declare that they have no competing interests.

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# Tables

**Table 1.** Clinical and pathological characteristics

| Variable | |
|---|---|
| N | 768 |
| Age (years), median (IQR) | 66 (58-75) |
| Sex (male/female) | 510/258 |
| BMI (kg/m$^2$), median (IQR) | 22.33 (20.20-24.22) |
| Tumor size (cm), median (IQR) | 4.12 (2.50-5.00) |
| Tumor location | |
| Gastric cancer | 312 (40.3%) |
| Colon cancer | 462 (59.7%) |
| Pathological type [n, (%)] | |
| Ulcerative | 564 (73.4%) |
| Non-ulcerative | 204 (26.6%) |
| Histopathological differentiation [n (%)] | |
| Well-differentiated | 573 (74.6%) |
| Poorly differentiated | 195 (25.4%) |
| Depth of invasion [n (%)] | |
| T1/T2 | 237 (30.9%) |
| T3/T4 | 531 (69.1%) |
| Lymph node metastasis [n (%)] | |
| Yes | 384 (50.4%) |
| No | 378 (49.6%) |

**Abbreviations:** IQR, interquartile range; BMI, body mass index.

**Table 2.** Relationship between preoperative serum markers and lymph node metastasis in patients with gastric and colon cancers

| Factors | Total | LMPG | LMNG | P-value |
|---|---|---|---|---|
| AFP(g/L) | 2.60 (2.00–3.60) | 2.60 (1.93–3.60) | 2.60 (2.00–3.60) | 0.921 |
| CEA(g/L) | 2.80 (1.60–7.30) | 3.10 (1.60–7.40) | 2.65 (1.70–6.70) | 0.687 |
| CA125(U/L) | 10.10 (7.15–15.95) | 11.20 (8.00–18.70) | 9.40 (6.70–13.40) | 0.008* |
| CA199(U/L) | 9.20 (5.00–16.60) | 9.45 (4.88–21.83) | 8.80 (5.10-14.50) | 0.136 |
| CA153(U/L) | 7.10 (5.10–10.20) | 7.10 (5.10–11.10) | 7.15 (5.40–9.40) | 0.828 |
| WBC（*$10^9$/L） | 6.00 (4.80–7.27) | 6.20 (4.90–7.80) | 5.80 (4.70–6.95) | 0.082 |
| Neutrophil（*$10^9$/L） | 3.60 (2.73–4.80) | 3.70 (2.80–5.30) | 3.40 (2.65–4.55) | 0.045* |
| Lymphocyte（*$10^9$/L） | 1.60 (1.20–2.00) | 1.50 (1.00–1.85) | 1.70 (1.20–2.00) | 0.066 |
| Hemoglobin(g/L) | 125.00 (108.25–138.00) | 121.00 (98.50–135.00) | 128.00(117.00–141.50) | 0.001* |
| RBC (*$10^{12}$/L) | 4.21 (3.73–4.70) | 4.14 (3.56–4.61) | 4.27 (3.88–4.71) | 0.014* |
| Platelet（*$10^9$/L） | 227.50 (183.25–281.75) | 230.00 (183.00–312.00) | 224.00 (183.50–264.50) | 0.174 |
| Albumin(g/L) | 38.15 (34.40–40.88) | 36.70 (33.80–40.15) | 38.85 (35.73–41.55) | 0.004* |
| NLR | 2.21 (1.67–3.53) | 2.37 (1.72–4.14) | 2.08 (1.63–3.04) | 0.015* |
| PLR | 145.62 (112.50–201.58) | 167.14 (113.88–226.46) | 136.00 (110.34–179.62) | 0.014* |

**Notes:** * Statistically significant (P<0.05). The values of the variables are presented as the median (IQR).

**Abbreviations:** IQR, interquartile range; AFP, alpha fetoprotein; CEA, carcinoembryonic antigen; CA-125, carbohydrate antigen 125; CA-199, carbohydrate antigen 199; CA-153, carbohydrate antigen 153; WBC, white blood cells; RBC, red blood cells; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMPG, lymph node metastasis positive group; LMNG, lymph node metastasis negative group.

**Table 3.** Univariate analysis of the risk of lymph node metastasis

| Factors | LMPG (n=384) | LMNG (n=378) | 2 | P-value |
|---|---|---|---|---|
| Sex | | | 0.096 | 0.757 |
| Men | 252 | 255 | | |
| Women | 132 | 123 | | |
| Age (years) | | | 0.244 | 0.621 |
| < 60y | 108 | 117 | | |
| ≧ 60y | 276 | 261 | | |
| BMI (kg/m$^2$) | | | 0.700 | 0.403 |
| < 24 | 312 | 291 | | |
| ≧ 24 | 72 | 87 | | |
| Tumor Size(cm | | | 24.314 | 0.000* |
| < 1.65 | 3 | 72 | | |
| ≧ 1.65 | 381 | 306 | | |
| Pathological type | | | 7.731 | 0.005* |
| Ulcerative | 312 | 249 | | |
| Non-ulcerative | 72 | 129 | | |
| Histopathological differentiation | | | 16.781 | 0.000* |
| Well-differentiated | 243 | 324 | | |
| Poorly-differentiated | 141 | 54 | | |
| Depth of invasion | | | 33.602 | 0.000* |
| T1/2 | 54 | 180 | | |
| T3/4 | 330 | 198 | | |
| S100 | | | 52.612 | 0.000* |
| Negative | 165 | 327 | | |
| Positive | 219 | 51 | | |
| CD31/D2–40 | | | 90.513 | 0.000* |
| Negative | 120 | 339 | | |
| Positive | 264 | 39 | | |
| MRP3 | | | 0.767 | 0.381 |
| Negative | 251 | 237 | | |
| Positive | 133 | 141 | | |
| EGFR | | | 0.570 | 0.450 |
| Negative | 199 | 229 | | |
| Positive | 185 | 149 | | |
| P53 | | | 0.578 | 0.188 |
| Negative | 128 | 147 | | |
| Positive | 256 | 231 | | |
| CDX2 | | | 0.001 | 0.970 |
| Negative | 17 | 17 | | |
| Positive | 367 | 361 | | |

**Notes:** *Statistically significant (P<0.05).

**Abbreviations:** LMPG, lymph node metastasis positive group; LMNG, lymph node metastasis negative group; BMI, body mass index; LMPG, lymph node metastasis positive group; LMNG, lymph node metastasis negative group.

**Table 4.** Multivariate analysis of lymph node metastasis in gastric cancer and colon cancer

| Factor | Gastric cancer | | Colon cancer | |
|---|---|---|---|---|
| | OR (95% CI) | P-value | OR (95% CI) | P-value |
| CA125(U/L) | - | | | |
| < 10.65 | | | Reference | |
| ≧ 10.65 | | | 2.660(1.087–6.509) | 0.032* |
| Albumin(g/L) | | | - | |
| < 36.8 | 7.804(1.791–34.003) | 0.006* | | |
| ≧ 36.8 | Reference | | | |
| PLR | - | | | |
| < 206.76 | | | Reference | |
| ≧ 206.76 | | | 3.896(1.436–10.572) | 0.008* |
| Histopathological | | | - | |
| Well-differentiated | Reference | | | |
| Poorly-differentiated | 3.601(0.935–13.869) | 0.066 | | |
| Depth of invasion | | | - | |
| T1/2 | Reference | | | |
| T3/4 | 5.982(1.599–22.373) | 0.008* | | |
| Nerve infiltration | - | | | |
| Negative | | | Reference | |
| Positive | | | 8.103(2.632–24.942) | 0.000* |
| Vascular infiltration | | | | |
| Negative | Reference | | Reference | |
| Positive | 29.251(6.665–128.37) | 0.000* | 9.177(3.113–27.056) | 0.000* |

**Notes:** *Statistically significant (P<0.05).

**Abbreviations:** CA-125, carbohydrate antigen 125; PLR, platelet-to-lymphocyte ratio; CI, confidence interval; OR, odds ratio.

**Table 5.** Multivariate analysis of lymph node metastasis in gastric and colon cancer

| Factor | OR | 95% CI | P-value* | Score |
|---|---|---|---|---|
| CA125 (U/L) | | | | |
| < 10.65 | Reference | | | 0 |
| ≧ 10.65 | 2.851 | 1.300–2.654 | 0.009 | 45 |
| Albumin (g/L) | | | | |
| < 36.8 | 2.334 | 1.000–5.450 | 0.050 | 37 |
| ≧ 36.8 | Reference | | | 0 |
| Hemoglobin (g/L) | | | | |
| < 116.5 | 3.255 | 1.369–7.738 | 0.008 | 51 |
| ≧ 116.5 | Reference | | | 0 |
| Pathological type | | | | |
| Ulcerative | 2.828 | 1.171–6.830 | 0.021 | 45 |
| Non-ulcerative | Reference | | | 0 |
| Tumor size (cm) | | | | |
| < 1.65 | Reference | | | 0 |
| ≧ 1.65 | 15.847 | 1.709–146.909 | 0.015 | 120 |
| Nerve infiltration | | | | |
| Negative | Reference | | | 0 |
| Positive | 2.812 | 1.209–6.536 | 0.016 | 45 |
| Vascular infiltration | | | | |
| Negative | Reference | | | 0 |
| Positive | 18.200 | 7.217–45.894 | 0.000 | 126 |

**Notes:** *All values in this column are statistically significant (P<0.05).

**Abbreviations:** CA-125, carbohydrate antigen 125; CI, confidence interval; OR, odds ratio.

**Table 6** Clinicopathologic characteristics of gastric and colon cancer patients, based on Score

| Factor | Score < 287 (432) | Score ≧ 287 (336) | 2 | P-value |
|---|---|---|---|---|
| Sex | | | 0.810 | 0.368 |
| Men | 297 | 213 | | |
| Women | 135 | 123 | | |
| Age (years) | | | 0.385 | 0.535 |
| < 60y | 135 | 93 | | |
| ≧ 60y | 297 | 243 | | |
| CA125 (U/L) | | | 11.136 | 0.001* |
| < 10.65 | 271 | 137 | | |
| ≧ 10.65 | 161 | 199 | | |
| Hemoglobin (g/L) | | | 9.207 | 0.002* |
| < 116.5 | 111 | 147 | | |
| ≧ 116.5 | 321 | 189 | | |
| Albumin (g/L) | | | 2.498 | 0.114 |
| < 36.8 | 162 | 159 | | |
| ≧ 36.8 | 270 | 177 | | |
| Pathological type | | | 20.185 | 0.000* |
| Ulcerative | 270 | 294 | | |
| Non-ulcerative | 162 | 42 | | |
| Histopathological | | | 28.871 | 0.000* |
| Well-differentiated | 378 | 195 | | |
| Poorly-differentiated | 54 | 141 | | |
| Tumor size (cm) | | | 21.871 | 0.000* |
| < 1.65 | 76 | 0 | | |
| ≧ 1.65 | 356 | 336 | | |
| Depth of invasion | | | 20.408 | 0.000* |
| T1/2 | 183 | 54 | | |
| T3/4 | 249 | 282 | | |
| Nerve infiltration | | | 76.307 | 0.000* |
| Negative | 378 | 117 | | |
| Positive | 54 | 219 | | |
| Vascular infiltration | | | 181.663 | 0.000* |
| Negative | 417 | 45 | | |
| Positive | 15 | 291 | | |
| Positive lymph node | | | 91.024 | 0.000* |
| < 4 | 420 | 150 | | |
| ≧ 4 | 12 | 186 | | |

**Notes:** *Statistically significant (P<0.05). The values in the table are the number of patients.

**Abbreviations:** CA-125, carbohydrate antigen-125.

# Figures

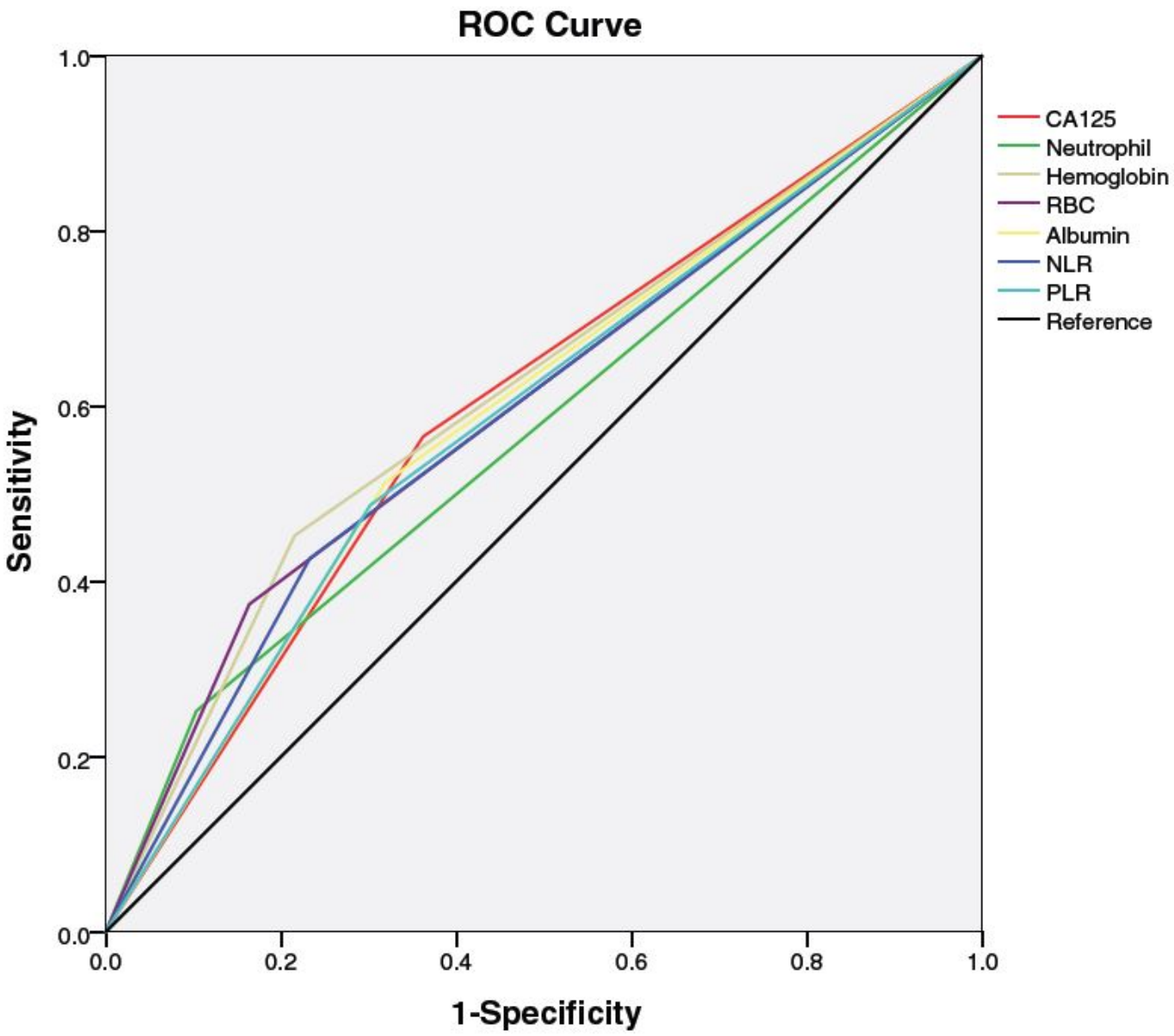
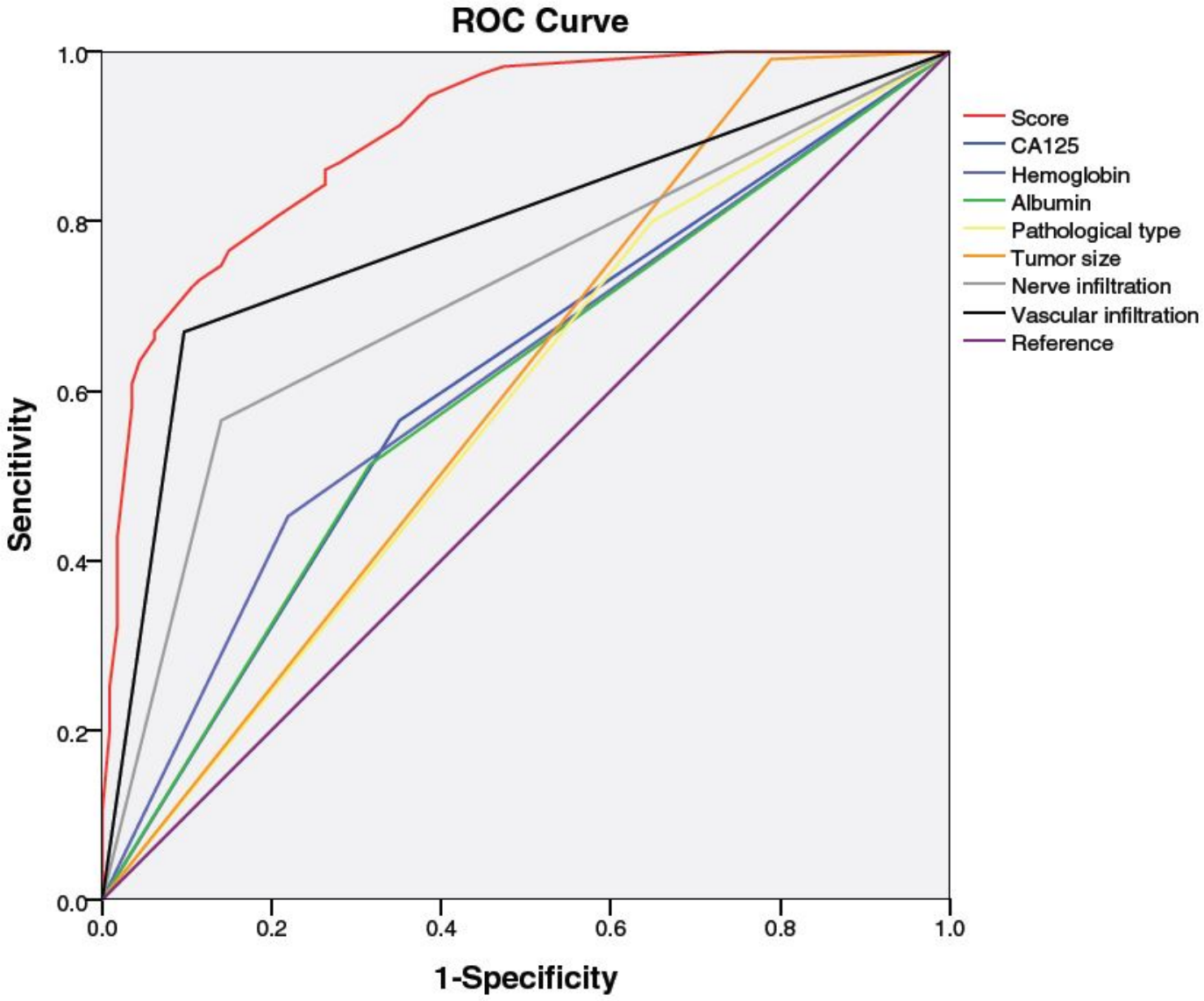


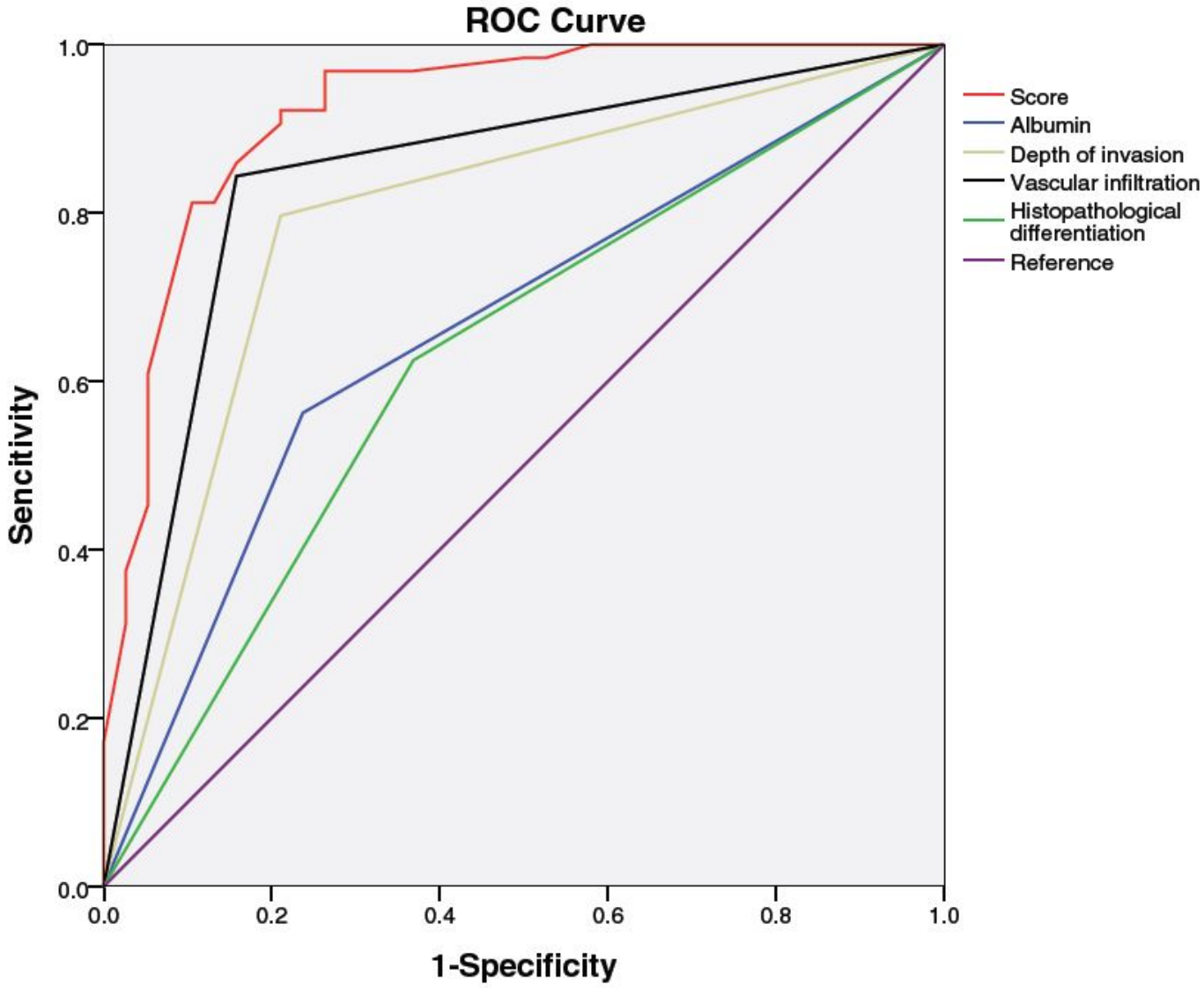

**Figure 1**

ROC curve for preoperative serum markers in patients with gastric and colon cancers according to lymph node metastasis.



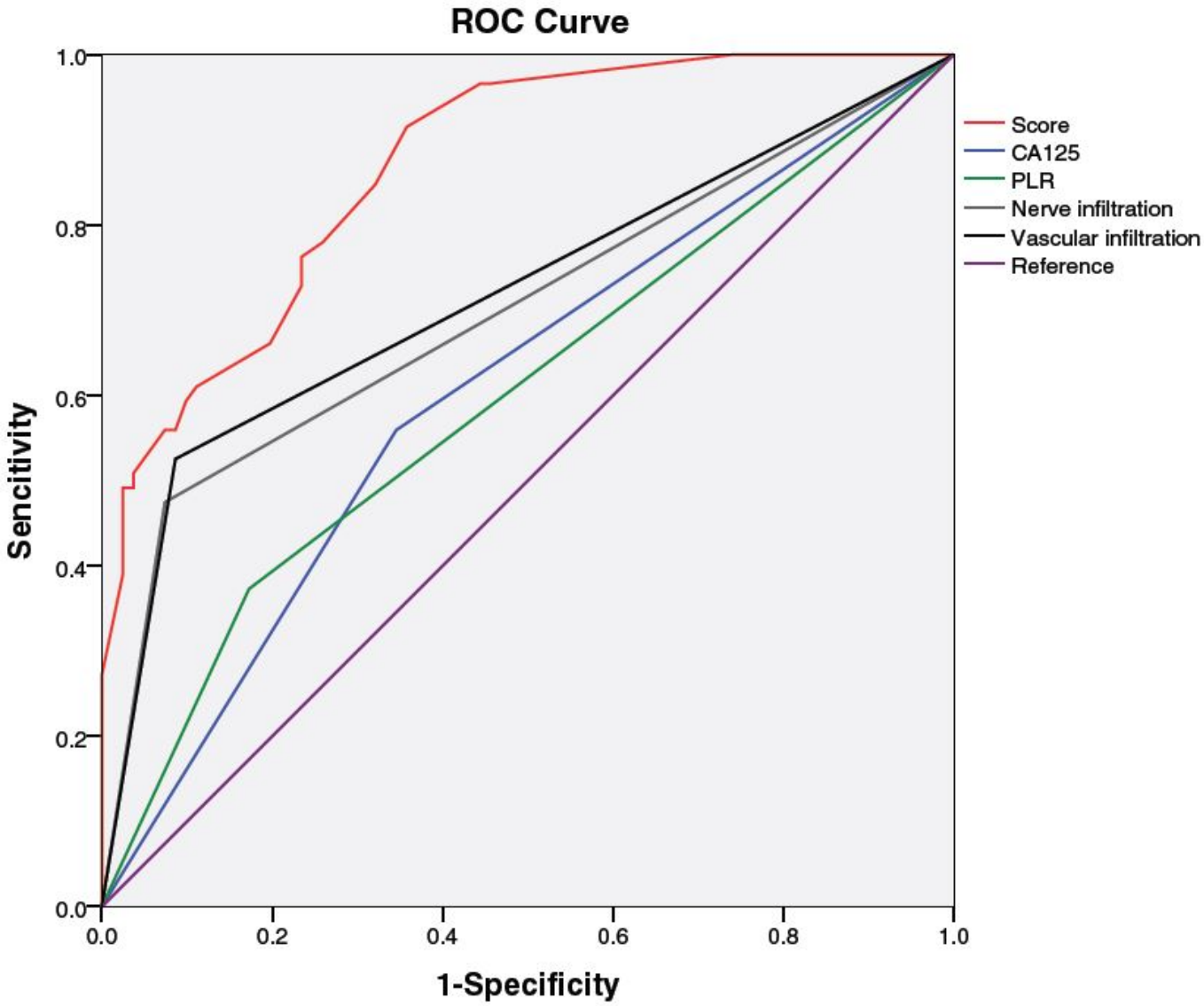

## Figure 2

Comparison of ROC curves for Score and the independent risk factors of gastric and colon cancer to evaluate the probability of lymph node metastasis.




## Figure 3

Comparison of ROC curves for Score and the independent risk factors of gastric cancer to evaluate the probability of lymph node metastasis.




## Figure 4

Comparison of ROC curves for Score and the independent risk factors of colon cancer to evaluate the probability of lymph node metastasis.