

The Value of ABO Blood Group and Complete Blood Count for the Prognosis Analysis of Gastric Cancer Patients

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Objective: To investigate the value of ABO blood group and complete blood count results in predicting the survival rate of patients with gastric cancer.

Patients and Methods: A retrospective study was conducted to collect 488 gastric cancer patients diagnosed in the Tumor Hospital Affiliated to Xinjiang Medical University from January 2010 to December 2011. Relevant clinical data were collected by the medical record system, and the patients were followed up by the medical record follow-up system of the hospital. The follow-up was ended until the death of the patients, and the survival time of all patients was obtained. Survival curve and Cox regression analysis model were used to study the role of various indicators in the prognosis of gastric cancer patients.

Results: Neutrophil lymphocyte ratio (NLR), neutrophil monocyte ratio (NMR), lymphocyte monocyte ratio (LMR) and platelet distribution width (PDW) in blood routine test could predict the death outcome of gastric cancer patients, with the predicted thresholds of 1.95, 13.49, 5.22 and 11.25, respectively. Survival curve analysis showed that female patients, type O blood patients, LMR >5.22 patients, NMR >13.49 patients and NLR ≤1.95 patients had longer survival. Multivariate Cox regression analysis model showed that gender and NLR were independent prognosis risk factors for gastric cancer, with HR values of 2.964 (95% CI of 2.258–3.891) and 1.103 (95% CI of 1.028–1.183), respectively. PLT and PDW were independent prognosis protective factors for gastric cancer, with HR values of 0.998 (95% CI of 0.997–1.000) and 0.891 (95% CI of 0.797–0.996), respectively. Compared with type O blood patients, patients with type A blood, type B blood and type AB blood had 3.472 times (95% CI 2.562–4.706), 3.368 times (95% CI 2.454–4.624) and 4.407 times (95% CI 2.871–6.766) increased risk of death.

Conclusion: The results of NLR, PLT, PDW and ABO blood group can help to predict the survival of gastric cancer patients.

Keywords: ABO blood group, complete blood count, gastric cancer, prognostic analysis

Introduction

Gastric cancer includes various tumors that occur in the stomach. More than 95% of these tumors come from epithelial cells, which named gastric cancer. There are also rare non-epithelial tumors in the stomach, including lymphoma and stromal tumors. In China, gastric cancer as the third highest incidence and the second highest death rate of malignant tumors has caused great damage to public health.¹ According to the literature, if early gastric cancer is limited to mucosa, the 5-year survival rate is about 90%; if only submucosal cancer is involved, the 5-year survival rate is about 85%; however, if

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gastric cancer is in middle, late stage or advanced stage, the 5-year survival rate is less than 40%.^{2,3} The clinical treatment of gastric cancer includes surgery, chemotherapy, targeted therapy, supportive treatment, etc. After receiving these treatment regimens, how to evaluate the prognosis of patients has important clinical significance for clinicians and patients, which can help clinicians to change the treatment regimens and improve the survival confidence of patients.

Complete Blood Count (CBC) is one of the most common Clinical laboratory examination project. Absolute counts of Neutrophils, Lymphocytes and Monocytes reflect the inflammatory response and the body's integral immune status. Inflammatory markers indicating prognosis in peripheral blood include the ratio of neutrophils to lymphocytes (NLR), the ratio of lymphocytes to monocytes (LMR), the ratio of platelets to lymphocytes (PLR), red blood cells distribution width (RDW) and platelet distribution width (PDW), these indicators have been proven to be closely related to the prognosis of a variety of cancers.^{4,5} ABO blood group also has been explored to be closely related to the prognosis of various malignant tumors.⁶ In clinical laboratories, the tests of CBC and ABO blood groups are inexpensive and required for every patients, so experimental data are relatively easy to obtain. Therefore, it has great clinical significance by the results of ABO blood group and CBC to predict the prognosis of gastric cancer patients.

Patients and Methods

Data Source

This retrospective study was approved by the ethics committee of Tumor Hospital Affiliated to Xinjiang Medical University, this study only used existing data of inpatients, and no interventions or injuries to patients, and all patient data confidentiality and compliance with the Declaration of Helsinki. So the patient consent to review their medical records was not required by the ethics committee of the tumor hospital affiliated to Xinjiang Medical University. The medical records of gastric cancer patients were allowed to be collected and analyzed. All the cases of gastric cancer were diagnosed by pathological results. A total of 488 cases gastric cancer were collected, including 281 males and 207 females in the Tumor Hospital Affiliated to Xinjiang Medical University from January 2010 to December 2011. The average age is 61 for men and 65 for women. At the same time, the results of the first CBC test and ABO blood type test on the first admission were collected, and the patients were followed up by the hospital's case follow-up system. The

outcome of the follow-up was the death of patients, and then obtained the survival time of all the patients.

Statistical Analysis

The area under the curve (AUC) was calculated by the receiver operating characteristic curve (ROC) and the optimal cutoff value of the continuous variable was calculated. The survival curves were compared by Kaplan–Meier method and Log-rank test. In addition, univariate and multivariate analyses were performed using Cox regression models to evaluate the effects of multiple covariates on survival outcomes. For all analyses, $P < 0.05$ was defined as significant. SPSS19.0 (SPSS, Chicago, IL) was used for statistical analysis.

Result

The General Clinical Features of 488 Gastric Cancer Patients

From Table 1, we can see that among the 488 gastric cancer patients, the proportion of male patients was significantly

Table 1 Analysis of 488 Gastric Cancer Patients

	Number of Cases	Constituent Ratio (%)
Gender		
Male	281	57.58
Female	207	42.42
Age		
<60 years old	169	34.63
≥60 years old	319	65.37
Helicobacter pylori infection		
Infection	310	63.52
No infection	178	36.48
TNM staging		
I/II	256	52.46
III/IV	232	47.54
CEA		
<5ng/mL	340	69.67
≥5ng/mL	148	30.33
CA199		
<37U/mL	388	79.51
≥37U/mL	100	20.49
Blood type		
Type O	217	44.47
Type A	133	27.25
Type B	100	20.49
Type AB	38	7.79

higher than female patients, and the proportion of patients over 60 years old was as high as 65.37%, and the infection rate of helicobacter pylori was as high as 63.52%. The positive rates of CEA and CA199, respectively, were 30.33% and 20.49%. Among the four blood groups of ABO, the detection rate of type O was the highest, up to 44.47%

The Critical Value of Each Detection Index

Taking the death of the patient as the final event. The ROC curve was used to find out whether there were appropriate critical values for every test item to predict the death outcome of the patients, so as to prove the significance of various indicators in the prognostic judgment. The quantitative indicators related to the outcome of the patient's death were respectively NLR, NMR, LMR and PDW. The ROC curves and related statistical results of various indicators are shown in Figure 1 and Table 2.

Survival Analysis Results of Every Significant Test Indicators

Using the survival curve to analyze the significance of gender, blood type and four quantitative indexes relating to the death outcome of gastric cancer patients to judge the prognosis of gastric cancer patients. The results are shown in Figure 2. It could be seen from Figure 2 that the survival period of female patients was longer than male

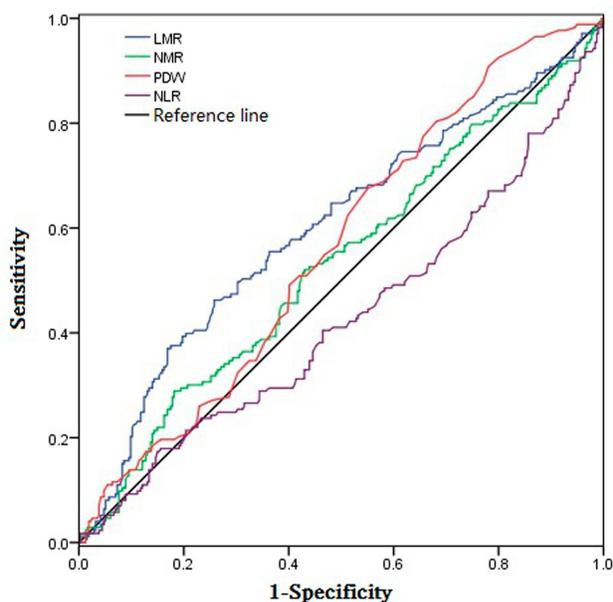


Figure 1 ROC analysis diagram of meaningful quantitative indicators.

Table 2 ROC Analysis Results of Significant Quantitative Indicators

Index	AUC	P value	Critical Value
NLR	0.572	0.009*	1.95
NMR	0.532	0.039*	13.49
LMR	0.601	<0.001*	5.22
PDW	0.563	0.021*	11.25

Note: *It has statistical significance.

patients ($P < 0.05$); the survival period of O-type blood patients was longer than other three types of non-O type blood patients ($P < 0.05$); Compared to $LMR \leq 5.22$ group and $NMR \leq 13.49$ group, in $LMR > 5.22$ group and $NMR > 13.49$ group, the patients' survival period were longer ($P < 0.05$), while $NLR \leq 1.95$ group was longer than that of $NLR > 1.95$ group ($P < 0.05$).

Univariate Cox Regression Analysis of Every Indicator

Univariate Cox regression analysis was used to calculate the value of gender, blood type and every quantitative indicator for the prognosis of gastric cancer (Table 3). It could be found that gender, blood type and NLR were the prognostic factors of gastric cancer. The risk of death in male patients was 1.825 times higher than female patients (95% CI 1.443–2.308). Compared to type O blood, patients with type A blood had a 2.107-fold increased risk of death (95% CI 1.536–2.648), the death risk of patients with type B blood increased by 2.094 times (95% CI 1.558–2.814), and the death risk of patients with type AB blood increased 2.372 times (95% CI 1.585–3.550). When the NLR value increased by 1, the risk of death increased by 1.062 times (95% CI 1.006–1.120).

Multivariate Cox Regression Analysis of Various Indicators

Multivariate Cox regression analysis was used to calculate the value of gender, blood type and every quantitative indicator on the prognosis of gastric cancer (Table 4). It could be found that gender, blood type and NLR were independent risk factors for the prognosis of gastric cancer. The risk of death in male patients was 2.964 times higher than female patients (95% CI 2.258–3.891). Compared with type O blood, the risk of death was 3.472 times higher in patients with type A blood (95% CI 2.562–4.706), that of patients with type B blood increased by 3.368 times (95% CI 2.454–4.624),

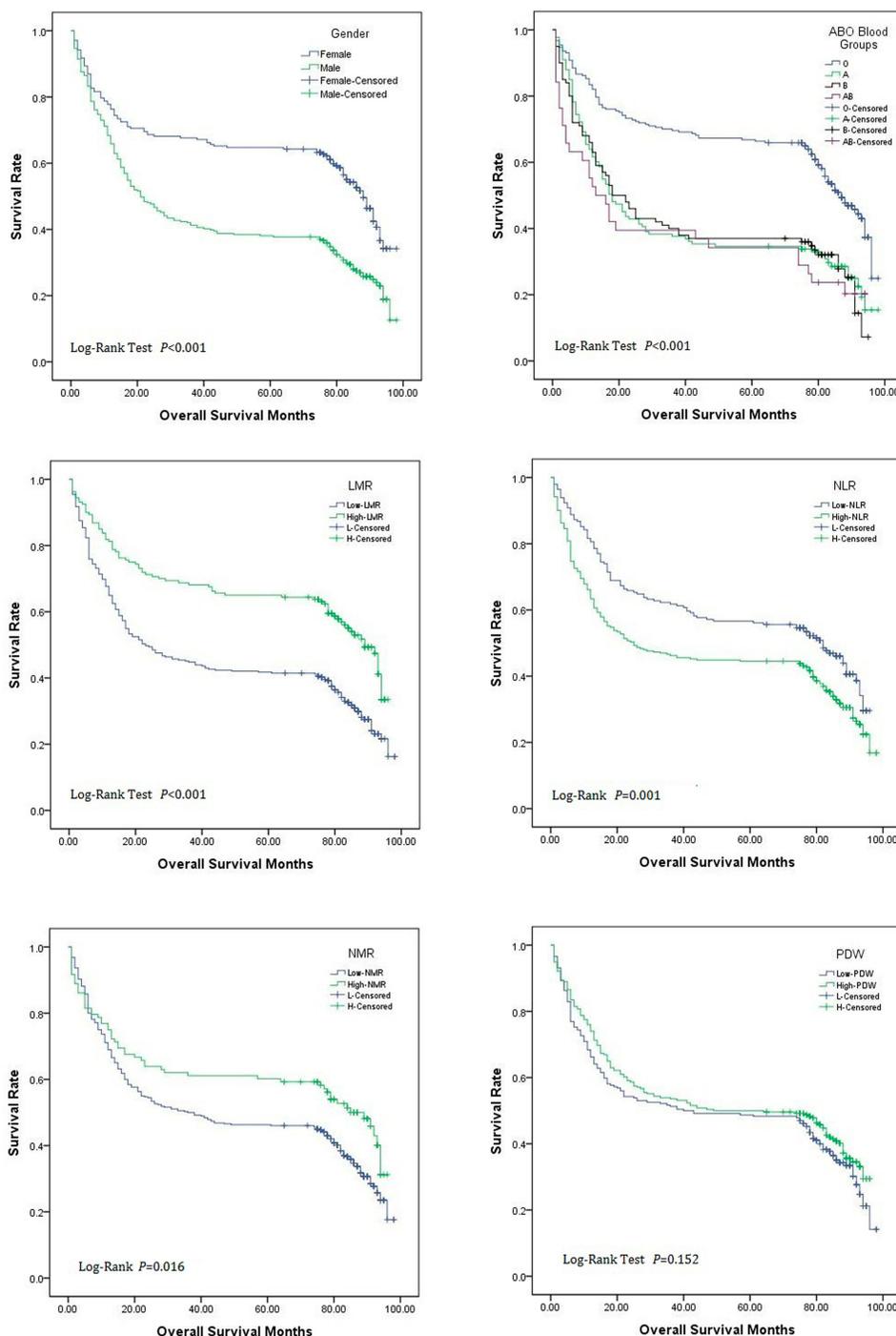


Figure 2 Analysis of survival curve of sex, blood group and meaningful clinical indexes.

and AB blood patients increased 4.407 times (95% CI 2.871–6.766). When NLR value increased by 1, the risk of death increased by 1.103 times (95% CI 1.028–1.183). While PLT and PDW were independent protective factors for the prognosis of gastric cancer, and the risk of death decreased by 0.998 times when PLT increased by 1 (95%

CI 0.997–1.000). The risk of death decreased by 0.891 times (95% CI 0.797–0.996), when PDW increased by 1.

Discussion

From the general data of 488 patients, it could be seen that male over 60 years old were more likely to suffer from

Table 3 Univariate Cox Regression Analysis Results of All Indicators

	β	Wald χ^2	P	HR	95% Confidence Interval
Gender (male/female)	0.601	25.147	<0.001*	1.825	1.443–2.308
ABO blood type					
A/O	0.701	25.454	<0.001*	2.107	1.536–2.648
B/O	0.739	23.993	<0.001*	2.094	1.558–2.814
AB/O	0.864	17.623	<0.001*	2.372	1.585–3.550
Hb	-0.001	0.061	0.804	0.999	0.995–1.004
PLT	-0.001	2.403	0.121	0.999	0.998–1.000
RDW	0.018	1.028	0.311	1.018	0.984–1.054
PDW	-0.036	2.118	0.146	0.965	0.919–1.013
PLR	-0.005	0.653	0.419	0.995	0.983–1.007
LMR	-0.005	0.558	0.455	0.995	0.982–1.008
NMR	0.000	0.001	0.978	1.000	0.994–1.006
NLR	0.060	4.796	0.029*	1.062	1.006–1.120

Note: *It has statistical significance.

Table 4 Cox Regression Analysis of Various Indicators

	β Value	Wald χ^2	P	HR	95% Confidence Interval
Gender (male/female)	1.087	61.197	<0.001*	2.964	2.258–3.891
ABO blood type					
A/O	1.245	64.417	<0.001*	3.472	2.562–4.706
B/O	1.214	56.443	<0.001*	3.368	2.454–4.624
AB/O	1.483	45.984	<0.001*	4.407	2.871–6.766
Hb	-0.002	0.346	0.556	0.998	0.993–1.004
PLT	-0.002	4.692	0.030*	0.998	0.997–1.000
RDW	0.013	0.335	0.563	1.014	0.968–1.061
PDW	-0.115	4.102	0.043*	0.891	0.797–0.996
PLR	0.020	1.927	0.165	1.020	0.992–1.049
LMR	0.002	0.049	0.825	1.002	0.985–1.019
NMR	-0.001	0.066	0.798	0.999	0.989–1.008
NLR	0.098	7.419	0.006*	1.103	1.028–1.183

Note: *It has statistical significance.

gastric cancer, and the infection rate of *Helicobacter pylori* in patients was as high as about 63.5%. Among the tumor markers commonly used in the laboratory, even the CEA and CA199 tumor markers recommended in the guidelines for the diagnosis and treatment of gastric cancer have a low positive rate in gastric cancer patients, which were

consistent with the existing reports.^{7,8} However, the existing reports showed that the incidence of blood group O was lower than non-O blood group in gastric cancer patients.^{9,10} But this study showed that the proportion of O blood group patients was the highest in 488 patients, which was inconsistent with the previous reports, it may be due to different population selection.

Many reports have shown that LMR, NLR and NMR, as inflammatory indicators, were closely related to the prognosis of various diseases.^{11,12} And could be used as prognostic factors for a variety of malignant tumors. For example, LMR and NLR could be used as prognostic indicators for esophageal cancer patients undergoing concurrent radiotherapy and chemotherapy.¹³ LMR could also be used as prognostic indicators for high-risk thyroid cancer.^{14,15} There were also some reports about the relationship between gastric cancer and these inflammatory indexes. Jinping et al reported that NLR could be used as a prognostic factor in patients with gastric cancer, and preoperative NLR >3.79 indicated a poor prognosis in patients with gastric cancer. It was also proved by Shumei et al.¹⁶ And the research results of Peng et al show that high NLR was an independent risk factor for the prognosis of postoperative cancer patients (HR 1.768–2.174).¹⁷ And the results of our study were generally in line with the above reports. It indicated that NLR was indeed an independent predictor of the prognosis of gastric cancer. At the same time, PLT and PDW were found to be independent protective factors for the prognosis of patients with gastric cancer. Ding Qunhua reported that reduced PDW before surgery was a poor prognosis factor of gastric cancer, which may become a prognostic indicator of gastric cancer.¹⁸ It was consistent with the results of this study that proved the important application value of platelet-related indicators in the prognosis of patients with gastric cancer.

ABO blood group system is one of the most widely used blood groups in clinical practice. In the past few years, some studies have reported that there may be a close relationship between ABO blood group and cancer risk. For example, A-type blood group could increase the incidence of a series of cancers, such as liver cancer, pancreatic cancer, ovarian cancer and nasopharyngeal cancer, and could predict the prognosis of some cancer patients.^{19–22} However, it has been reported that ABO blood group was only related to the occurrence of gastric cancer, and has no correlation with the prognosis of gastric cancer patients.^{23–25} Due to the fact that there was a correlation between ABO blood group and the

prognosis of most malignant tumors, this study restudied the correlation between ABO blood group and gastric cancer. It was found that ABO blood group was also a good independent prognostic factor for gastric cancer, especially compared to gastric cancer patients with O blood group, and the patients with non-O blood groups had a higher risk of death. The direct biological mechanism of the relationship between ABO blood group and many kinds of tumors, including gastric cancer, was still inconclusive, but some hypotheses could explain this relationship. Firstly, the ABO gene was located on chromosome 9q and formed from seven exons, which encodes a glycosyltransferase that catalyzes the transfer of carbohydrates and binds to H antigen to form an antigenic structure of ABO blood group. Blood group antigens are expressed not only on the surface of red blood cells, but also in many other tissues, it has been proven that the modified expression of blood group antigen on the surface of tumor cells could change the motility, drug resistance, apoptosis and immune escape ability of tumor cells. In addition, because there was a high positive correlation between AB blood group and the circulating level of soluble intercellular adhesion molecule-1 (sICAM-1), and a high level of sICAM-1 contributes to the immune escape of malignant tumors, patients with O blood group are less likely to have a poor prognosis due to the lack of corresponding blood group antigens.^{26,27} The results of this study on the relationship between ABO blood group and the prognosis of gastric cancer were contradictory to previous reports, and more studies are needed to verify which conclusion is more correct.

Conclusion

The related indexes of CBC and ABO blood group test, as cheap indexes in clinical laboratory, have a certain significance in judging the prognosis of patients with gastric cancer. However, because the laboratory test results of CBC related indexes are too uncontrollable factors and the degree of variation of the indexes is too large, the role of CBC in the judgment of clinical prognosis is limited. While the results of ABO blood group system are constant, more research should be carried out in judging the prognosis of patients with gastric cancer in the future.

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Disclosure

The authors declare that they have no conflicts of interest.

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