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Retrospective Study

Development and validation of a novel nomogram for predicting overall survival in gastric cancer based on inflammatory markers

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Abstract

BACKGROUND

Nearly 66% of occurrences of gastric cancer (GC), which has the second-highest death rate of all cancers, occur in developing countries. In several cancers, the predictive significance of inflammatory markers has been established.

AIM

The objective of this research was to look into extensive clinical characteristics and develop a specific nomogram to determine overall survival for GC patients.

METHODS

Nine hundred and four GC patients in the First Affiliated Hospital of Anhui Medical University between January, 2010 and January, 2013 were recruited. Prognostic risk variables were screened for using Cox analysis. The C index, receiver operator characteristic (ROC) curve, and decision curve analysis are used to evaluate the nomogram.

RESULTS

Tumor Node Metastasis stage, carcinoembryonic antigen, systemic immune-inflammation index (SII), and age were identified as independent predictive variables by multivariate analysis. SII value was superior to that of other inflammatory indicators. The ROC indicated the nomogram had a higher Area Under Curve than other factors, and its C-index for assessing the validation and training groups GC patients was extremely reliable.

CONCLUSION

We created a novel nomogram to forecast the prognosis of GC patients following curative gastrectomy based on the blood markers and other characteristics. Both surgeons and patients can benefit significantly from this new scoring system.

Key Words: Gastric cancer; Nomogram; NLR; PLR; SII

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Core Tip: 1 According to our study, the prognosis of patients with gastric cancer was significantly influenced by systemic immune-inflammation index, Carcinoembryonic antigen, Tumor Node Metastasis stage, and age. 2 We created a novel nomogram to forecast the prognosis of gastric cancer patients following curative gastrectomy based on the blood markers and other characteristics. Both surgeons and patients can benefit significantly from this new scoring system.

INTRODUCTION

Nearly 66% of instances of gastric cancer (GC), which has the second-highest death rate of all cancers[1], occur in the developing countries[1,2]. The only curative treatment for patients is considered to be a radical surgery, which increases the likelihood of a successful cure and lengthens patient survival. The high likelihood of cancer recurrence, however, means that the 5 years Overall Survival (OS) is still poor even after a surgery[3]. The Tumor Node Metastasis (TNM) stage are connected with the prognosis of GC patients, but it's difficult to get it prior to surgery. Carcinoembryonic antigen (CEA) is one of the most often utilised serum indicators in relation to stomach cancer, according to research that have been conducted recently[4,5,6]. In order to diagnose cancer and predict for recurrences following surgery, CEA has been employed[4]. The neutrophils to lymphocytes ratio (NLR) and the platelets to lymphocytes ratio (PLR) are two additional blood indices that can be used to assess the prognosis of malignancy[5,6,7]. Additionally, the level of haemoglobin is related to a patient's prognosis[8]. The purpose

of this study is to identify additional clinical blood indicators that may be used to evaluate GC patients prognosis and create a trustworthy scoring system.

There has been much research on the connection between cancers and inflammation. Cancer brought on by inflammation has been shown to damage DNA and create microscopic metastases[9]. The body's immune system may become less effective and tumour growth may be accelerated by the systemic inflammatory response (SIR). According to related study, lymphocyte (LY), platelet (PLT), and neutrophil (NE), all have a great impact on SIR, which is linked to tumour formation[10,11]. The predictive usefulness of many systemic inflammation factors, such as NLR-PLR[12], PLT-NLR[13], and systemic immune-inflammation index (SII), has been well established in various malignancies[14,15]. There hasn't been any clinical research published comparing the prognostic significance of different scoring systems. In this study, we set out to investigate additional clinical blood indicators and create a strong nomogram for predicting OS following gastrectomy.

MATERIALS AND METHODS

Patients

From January, 2010 to January, 2013, 904 GC patients admitted to the First Affiliated Hospital of Anhui Medical University provided blood samples and clinical data. All chosen participants were randomly divided into training (n = 543) and validation (n = 361) cohorts for the study's final analysis. Our hospital's Institutional Review Board and Ethical Committee have given their approval for this study.

Inclusion and exclusion criteria

The criteria for admission included: (1) A histological diagnosis indicated that is GC; (2) The malignancy has been definitively and entirely removed after surgery; (3) All of the patients' peripheral blood tests were completed within two d after the operation; and (4) None of the patients experienced multiple organ failures. Patients were excluded if they met any of the following criteria: (1) They had other primary tumours; (2) They

had undergone radiotherapy and chemotherapy prior to surgery; (3) They had any diseases that could interfere with peripheral blood cells, such as infections; and (4) they had passed away within one mo after operation. Finally, a cohort of 904 gastric cancer patients was examined.

Data collection and follow-up

Through the medical records department, information on the patient's age, gender, differentiation grade, tumour size, and other characteristics as well as clinical pathology was acquired. The following is a list of the laboratory results: NE, LY, and PLT, *etc*. 3 d before the operation, peripheral blood was analysed, the CEA and haemoglobin cutoff values were obtained based on normal levels, and the median was used to determine the NE, LY, and PLT cutoff values. SII was calculated by platelet count × NE count/LY count. According to the ideal cut-off values, which were determined using the Youden index [maximum (sensitivity + specificity - 1)][16], they were divided into low and high group. For NLR–PLR assignment, (high NLR) + (high PLR) = 2; (only one high group) = 1; (low NLR) + (low PLR) = 0. The assignment of NLR-PLT is also similar to the above method.

Statistical analysis

The categorical values were counted by Chi-square test or Fisher exact test, and continuous variables were analyzed by Student's T test. The Cox appropriate hazard model was used to perform both multivariate and univariate survival analyses. In order to assess the accuracy of the prognostic model, the C-index and receiver operator characteristic (ROC) were utilized. R Studio and SPSS program (version 19.0) were used for the full data analysis process.

RESULTS

ROC curve of SII, NLR, and PLR

By using the ROC curve of the greatest Youden index, we calculate the pre-operative NLR, PLR, and SII value. Based on the Youden index, the optimal cutoff value of NLR, PLR, SII was calculated to be 2, 160 and 475.6, respectively.

Clinical characteristics of training and validation groups

Table 1 showed the clinical data of 904 GC patients (Training group accounts for 543, validation group accounts for 361), and the training groups and validation groups had no statistically difference ($P > 0.05$).

Univariate and multivariate analysis of training cohort

Prognostic factors identified by univariate analysis were gender, hemoglobin, age, TNM, NLR, tumor size, PLR, SII, and CEA (Table 2). Multivariate analysis revealed that age, CEA, SII, and TNM were independent predictive factors for GC patients (Table 3).

The ROC curve of inflammatory markers

We used the ROC curve to compare the utility of all the inflammatory indicators in GC patients (Figure 1). The AUC for SII was bigger than that of NLR, NLR-PLT, PLR as well as NLR-PLR.

Nomogram for OS

A novel nomogram was created to predict the OS of GC based on the multivariate analysis result (Figure 2). Table 4 revealed the nomogram scoring method.

Validation of the nomogram model in training group and validation group

We applied calibration curves to verify the model in the training and validation group (Figure 3-6). In the training group, the nomogram's C-index was 0.736, whereas in the validation group, it was 0.651. In order to further demonstrate the nomogram performance, we displayed the ROC of the nomogram (Figure 7). In addition, the AUC of the nomogram is large, showing nomogram is dependable.

Decision Curve Analysis (DCA) of the nomogram in training and validation group

DCA results indicate the clinical use of the novel model for estimating 3-5 years survival in GC patients in the training group and validation group (Figure 8-11).

The Kaplan-Meier curves in training group

The training group was then separated into three sub-groups depending on the cutoff value (< 60 was low risk; 60–120 was medium risk; > 120 was high risk). The Kaplan-Meier curve demonstrated the good outcomes (Figure 12).

DISCUSSION

The only curative form of treatment for gastric cancer is generally believed to be surgery. Early GC is typically difficult to diagnose due to the limitations of available procedures. The 5-year survival rate at the moment is quite poor. As a result, several researchers have worked to enhance the prognosis for GC patients. TNM stage and lymph node metastases were identified as important independent risk factors, however, because it is challenging to evaluate these prognostic factors prior to surgery, substantial research has been done recently on serum markers. This study, to the best of our knowledge, is the first to compare the serum score system and then create a novel nomogram that combines peripheral blood markers and clinical factors to predict OS for one year, three years, and five years.

The results demonstrated that age, SII, TNM stage, and CEA were each independent predictors of gastric cancer patients. SII was a more effective indicator to predict OS based on the fact that its AUC was higher than that of NLR-PLR and NLR-PLT. The C-index of our newly constructed nomogram, which was based on independent prognostic variables, was 0.736, indicating that it is quite accurate in predicting GC patients' prognoses. This nomogram is an accurate score system because the DCA curve and calibration curves both supported its clinical use. Nomograms are more valuable than TNM stages for predicting prognosis in several cancers[17,18]. Since

the nomogram's AUC in this study is higher than other element, surgeon may use this scoring system to more accurately assess the patient's prognosis and choose the most beneficial course of action in the clinic.

Four factors in our nomogram were significantly influenced by SII. According to recent studies, inflammation may have an impact on the development of cancer and long-term survival of patients[19]. SII, which may include NE count, PLT count, and LY count, was among them but was less frequently reported. NLR-PLT and NLR-PLR were associated with GC patients' prognosis, whereas SII was an independent prognostic factor and had higher value. Our study proved that CEA was a reliable prognostic factors and that it may be used to screen for cancer recurrence. As a result, we need to pay more attention to patients who have elevated levels of CEA. Age was another important prognostic factor, and this result was consistent with earlier research[20]. With the increase of age, the immunity of elderly patients decreases significantly, which leads to the recurrence and metastasis of cancer easily, thus making elderly patients with GC have a worse outcome. As a result, these important factors need to be given more emphasis in order to improve patient outcomes, and the nomogram may be used more frequently in clinics.

CONCLUSION

In conclusion, our research showed that the age, SII, TNM stage, and CEA were major factors of the prognosis for GC patients, and the new nomogram was a valid prognostic tool for them.

ARTICLE HIGHLIGHTS

Research background

Nearly 66% of instances of gastric cancer (GC), which has the second-highest death rate of all cancers, occur in the developing countries. The only curative treatment for patients is considered to be a radical surgery, which increases the likelihood of a successful cure and lengthens patient survival. The high likelihood of cancer recurrence,

however, means that the 5-year OS is still poor even after a surgery. The TNM stage are connected with the prognosis of GC patients, but it's difficult to get it prior to surgery.

Research motivation

To investigate more clinical characteristics and develop a specific nomogram to forecast OS for GC patients.

Research objectives

Nine hundred and four GC patients in the First Affiliated Hospital of Anhui Medical University between January, 2010 and January, 2013 were recruited.

Research methods

Prognostic risk variables were screened for using Cox analysis. The C index and ROC curve are used to construct and evaluate the nomogram.

Research results

TNM stage, CEA, SII, and age were identified as independent predictive variables by multivariate analysis. SII value was superior to that of other inflammatory indicators. The ROC indicated the nomogram had a higher AUC than other factors, and its C-index for assessing the validation and training groups GC patients was extremely reliable.

Research conclusions

We created a novel nomogram to forecast the prognosis of GC patients following curative gastrectomy based on the blood markers and other characteristics.

Research perspectives

Both surgeons and patients can benefit significantly from this new scoring system. and the nomogram may be used more frequently in clinics.

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