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Nomogram for predicting the prognosis of tumor patients with sepsis after gastrointestinal surgery

Ren-Xiong Chen, Zhou-Qiao Wu, Zi-Yu Li, Hong-Zhi Wang, Jia-Fu Ji

Abstract

BACKGROUND

There were few studies on the prognosis of tumor patients with sepsis after gastrointestinal surgery and there was no relevant nomogram for predicting the prognosis of these patients.

AIM

To establish a nomogram for predicting the prognosis of tumor patients with sepsis after gastrointestinal surgery in the intensive care unit (ICU).

METHODS

A total of 303 septic patients after gastrointestinal tumor surgery admitted to the ICU at Peking University Cancer Hospital from January 1, 2013 to December 31, 2020 were analysed retrospectively. The model for predicting the prognosis of septic patients was established by the R software package.

RESULTS

The most common infection site of sepsis after gastrointestinal surgery in the ICU was abdominal infection. The 90-d all-cause mortality rate was 10.2% in our study group. In multiple analyses, we found that there were statistically significant differences in tumor type, septic shock, the number of lymphocytes after ICU admission, serum creatinine and total operation times among tumor patients with sepsis after gastrointestinal

surgery (P < 0.05). These five variables could be used to establish a nomogram for predicting the prognosis of these septic patients. The nomogram was verified, and the initial C-index was 0.861. After 1000 internal validations of the model, the C-index was 0.876, and the discrimination was good. The correction curve indicated that the actual value was in good agreement with the predicted value.

CONCLUSION

The nomogram based on these five factors (tumor type, septic shock, number of lymphocytes, serum creatinine, and total operation times) could accurately predict the prognosis of tumor patients with sepsis after gastrointestinal surgery.

Key Words: Tumor; Surgery; Sepsis; Gastrointestinal; Nomogram

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Core Tip: There were few studies on the prognosis of tumor patients with sepsis after gastrointestinal surgery and there was no relevant nomogram for predicting the prognosis of these patients. The aim of the study was to establish a nomogram for predicting the prognosis of tumor patients with sepsis after gastrointestinal surgery in the intensive care unit (ICU).The most common infection site of sepsis was abdominal infection and the 90-d all-cause mortality rate was 10.2% in our study group. In multiple analyses, we found that there were statistically significant differences in tumor type, septic shock, the number of lymphocytes after ICU admission, serum creatinine and total operation times among tumor patients with sepsis after gastrointestinal surgery (P < 0.05). These five variables could be used to establish a nomogram for predicting the prognosis of these septic patients. The nomogram was verified, and the initial C-index

was 0.861. After 1000 internal validations of the model, the C-index was 0.876, and the discrimination was good. The correction curve indicated that the actual value was in good agreement with the predicted value.

INTRODUCTION

Since the definition of sepsis in version 1.0 (infection + systemic inflammatory response syndrome) was too sensitive and the specificity was poor and the definition of sepsis in version 2.0 was too cumbersome, the new definition of sepsis was life-threatening organ dysfunction caused by the imbalance of host response to infection, which was manifested in an increase in sequential organ failure score (SOFA) by more than one point[1]. Septic shock was identified as sepsis with severe circulatory, cellular and metabolic disorders, while its mortality was significantly higher than that of sepsis. Septic shock was mainly characterized by continuous hypotension with tissue hypoperfusion (lactic acid > 2 mmol/L).

The incidence rate of sepsis was notably high and mortality was especially high. It is estimated that tens of millions of septic patients die worldwide every year[2,3]. Sepsis not only increased the hospitalization expenses of patients but also prolonged the hospitalization time of patients. According to statistics, the total hospitalization cost of sepsis has jumped first in the United States, with an annual cost of approximately 38.2 billion United States dollars[4]. Therefore, we should pay more attention to the prevention and treatment of sepsis.

The predisposing factors of sepsis include community infection and nosocomial infection, and the mortality of septic patients induced by nosocomial infection is often higher[5,6]. Early identification of infection, infection source control, appropriate application of antibiotics and aggressive volume resuscitation of critically ill patients were the cornerstones of septic patient management[7-10]. These factors had a major influence on the prognosis of septic patients. It is well known that many factors could affect the prognosis of septic patients. However, there were few factors widely used to predict the prognosis of septic patients and there was no relevant nomogram for

predicting the prognosis of these patients. In this study, we first retrospectively analysed 303 septic patients after gastrointestinal tumor surgery, collected some factors, analysed their relationship with prognosis, and then established a model for predicting the prognosis of these septic patients.

MATERIALS AND METHODS

Study population

The study which was registered at the Chinese Clinical Trial Registry (registration ID: ChiCTR2100051826) was conducted according to the Declaration of Helsinki (as revised in 2013). Ethical approval for the study was obtained from the Medical Ethical Committee of Peking University Cancer Hospital (ethics approval number 2020KT33) and informed consent from all the septic patients or their relatives. Inclusion criteria: From January 1, 2013 to December 31, 2020, a total of 4731 patients were admitted to the intensive care unit (ICU) at Peking University Cancer Hospital, of which 2448 patients were transferred to the ICU for various reasons (complicated with chronic medical diseases, sepsis, bleeding, acute myocardial infarction, acute heart failure, acute pulmonary embolism, acute cerebral infarction, pneumothorax, *etc.*) after gastrointestinal tumor surgery in the gastrointestinal tumor center. According to the new definition of sepsis, 303 septic patients were included in our study. Exclusion criteria: those patients without surgery; postoperative patients with non-gastrointestinal tumors; patients without sepsis. The flow diagram is shown in Supplementary Figure 1.

The treatment of septic patients before 2016 mainly referred to the 2012 version of sepsis/septic shock guidelines[11], while the treatment of septic patients after 2016 mainly referred to the 2016 version of sepsis/septic shock guidelines[7]. For patients whose final culture results were negative, at least two experts would finally determine the most likely infection source of the patients after discussion.

For abdominal sepsis, we controlled the source of infection actively through minimally invasive drainage or surgical debridement by a multidisciplinary team.

Data collection and follow up

Clinical data and some laboratory tests of septic patients after gastrointestinal surgery were collected. Baseline information included age, body mass index (BMI), basic diseases, chronic diseases, Charlson score and tumor type. Clinical diagnosis and treatment data included whether the first operation was an emergency operation, laparoscopic or open in the first operation, the length of the first operation, drug sensitivity test results, antibiotics used, septic shock, number of blood leukocytes, number of lymphocytes, percentage of lymphocytes, percentage of neutrophils, activated partial thromboplastin time (APTT), albumin, serum creatinine, cardiac troponin I (cTnI), procalcitonin (PCT), blood lactic acid, oxygenation index (PaO2/FiO2), SOFA within 24 h after ICU admission, whether had gastrointestinal fistula or perforation and total operation times. Except for specially specified data, other data were the first data collected in the ICU.

The survival time of septic patients was calculated from entering the ICU and followed up to 90 d. If the patient's death occurred before 90 d, he was followed up to the day of death. Follow-up was carried out through an inpatient electronic case system or telephone and patient's survival status was recorded.

Statistical analyses

The data were processed by the R3.6.3 software package. Continuous variables were statistically described as the means ± SD and discontinuous variables were described by medians (Q1, Q3). The enumeration data were expressed as numerical values (percentages).

Univariate analysis was performed by the log rank test. Those factors with $P < 0.05$ in the univariate analysis were included in the multiple analysis and Cox regression analysis was used. Statistically significant factors in multiple survival analysis were used to establish a nomogram for predicting the prognosis of septic patients with the R3.6.3 software package. The performance of the model was evaluated by the C-index and calibration curve. The bootstrap method was used for the internal verification of

the model. Two sided tests were used for all statistical analyses, and the statistical test $P < 0.05$ represented that the difference was statistically significant.

RESULTS

Patient characteristics

According to the new definition, 303 tumor patients were diagnosed with sepsis after gastrointestinal surgery, including 119 patients who needed vasopressors who were diagnosed with septic shock. The median age of these septic patients was 66 years. The most common complication was hypertension, followed by diabetes. According to the classification of tumor types, there were 138 patients with gastric cancer, 148 patients with colorectal cancer and 17 patients with other abdominal and pelvic tumors (5 cases of gastrointestinal stromal tumors, 4 cases of lymphoma, 2 cases of melanoma, 2 cases of implanted intestinal wall of ovarian cancer, 1 case of cervical cancer with postoperative intestinal perforation, 1 case of ileal metastasis of renal cancer, 1 case of abdominal fibromatosis and 1 case of colonic adenoma).

Among these septic patients, 35 underwent emergency surgery and 268 underwent limited surgery for the first operation. The median time of the first operation was 180 minutes. In the course of treatment, 24 patients with sepsis were complicated with abdominal bleeding or gastrointestinal hemorrhage, 28 patients with venous thrombosis (including 9 cases of acute pulmonary embolism), 2 patients with acute cerebral infarction, 2 patients with acute myocardial infarction and 1 patient with cerebral hemorrhage. A total of 12 patients needed continuous renal replacement therapy due to renal failure, 149 patients received ventilator treatment and 1 patient received extracorporeal membrane oxygenation. The baseline information is shown in Table 1.

Pathogenic microorganisms in patients with sepsis

The most common infection site of sepsis after gastrointestinal surgery was abdominal infection, followed by pneumonia. Pathogenic microorganisms could be isolated in 255

cases (84.2%) of these septic patients, however 48 cases (15.8%) could not. Gram-negative bacilli (197 cases) were the most common pathogenic microorganisms, followed by gram-positive cocci (100 cases), fungi (28 cases) and gram-positive bacilli (2 cases). See Supplementary Table 1 for the microorganisms in each infection site.

The common isolated pathogens were as follows (≥ 5 cases): Ninety-seven cases of Escherichia coli, 50 cases of Pseudomonas aeruginosa, 40 cases of Klebsiella pneumoniae, 30 cases of Enterococcus faecalis, 22 cases of Candida albicans, 20 cases of Enterococcus faecium, 12 cases of Staphylococcus aureus, 11 cases of Acinetobacter baumannii, 11 cases of Stenotrophomonas maltophilia, 10 cases of Streptococcus pharyngitis, 9 cases of Enterococcus avium and 8 cases of Staphylococcus epidermidis, 7 cases of hemolytic Staphylococcus, 7 cases of Klebsiella aerogenes and 6 cases of Enterobacter cloacae.

The distribution of common drug-resistant bacteria isolated was as follows: Seventy cases of Escherichia coli producing extended spectrum β-lactamase (ESBL) and 7 cases of Klebsiella pneumoniae producing ESBL; 11 cases of carbapenem resistant Pseudomonas aeruginosa, 3 cases of carbapenem resistant Acinetobacter baumannii, and 2 cases of carbapenem resistant Enterobacteriaceae; 7 cases of methicillin resistant Staphylococcus epidermidis, 6 cases of methicillin resistant Staphylococcus aureus and 5 cases of methicillin resistant hemolytic Staphylococcus; 2 cases of vancomycin resistant enterococci.

Survival analysis of patients with sepsis

Three hundred and three septic patients were followed up for 90 d. A total of 31 patients died (27 patients died of multiple organ failure caused by septic shock, 2 patients died of hemorrhagic shock, 1 patient died of intracerebral hemorrhage and 1 patient died of respiratory failure). The 90 d all-cause mortality was 10.2%. Since there were slight differences in the sepsis/septic shock guidelines for the treatment of septic patients before and after 2016, we first performed a comparative analysis of the survival

rate of septic patients before and after 2016. There was no significant difference in the 90-d survival rate among septic patients before and after January 1, 2016 ($P = 0.415$).

The univariate survival analysis showed that there were statistically significant differences in BMI, tumor type, empirical anti-infection evaluation, septic shock, number of lymphocytes after entering the ICU, the activated prothrombin time after entering the ICU, blood creatinine, PCT, blood lactic acid, oxygenation index, SOFA score within 24 h after entering the ICU and total operation times ($P < 0.05$). See Table 2 for the results of univariate analysis of these septic patients.

The twelve factors with $P < 0.05$ in univariate analysis were included in multiple analyses. The results showed that there were significant differences in tumor type, whether there was septic shock, number of lymphocytes after entering the ICU, serum creatinine and total operation times on the prognosis of these septic patients ($P < 0.05$). The areas under the receiver operating characteristic (ROC) curve of these five factors predicting the prognosis of postoperative sepsis of gastrointestinal tumors were 0.614, 0.766, 0.574, 0.629, and 0.513, respectively. The results of multiple analyses of tumor patients with sepsis after gastrointestinal surgery are shown in Table 3.

The 90-d survival rate of patients with postoperative sepsis of gastric cancer was worse than that of patients with postoperative sepsis of colorectal cancer ($P = 0.003$). However, there was no statistically significant difference in the survival rate between patients with postoperative sepsis of gastric cancer and patients with postoperative sepsis of other abdominal and pelvic tumors ($P = 0.739$). The 90-d survival rate of patients with postoperative sepsis of gastrointestinal tumors who underwent three operations was lower than that of patients who underwent only one operation ($P = 0.005$). However, there was no significant difference in the survival rate between patients with postoperative sepsis of gastrointestinal tumors who underwent two operations and patients who underwent only one operation ($P = 0.105$).

A nomogram for predicting the prognosis of patients with sepsis

The five factors affecting the 90-d survival rate of patients with postoperative sepsis of gastrointestinal tumors screened by Cox regression analysis were included in the prediction of the prognosis model. A nomogram for predicting the prognosis of patients with postoperative sepsis of gastrointestinal tumors was established and output by R statistical software (Figure 1). In clinical application, we found the corresponding value of each predictor in the nomogram and added the scores of each predictor to the total score. Finally, the total score was read on the axis of 90-d overall survival rate, which was the 90-d survival probability of the patient.

Discrimination of the nomogram

We used the C-index to evaluate the differentiation of a nomogram for predicting the prognosis in septic patients after gastrointestinal surgery. The initial C-index of the nomogram was 0.861 and the 95%CI was 0.809-0.913, indicating that the nomogram for predicting the prognosis in septic patient after gastrointestinal tumor surgery had good discrimination.

Calibration

The calibration of the nomogram for predicting the prognosis in septic patients after gastrointestinal surgery was carried out through the correction curve. The correction curve revealed that the observed value was consistent with the predicted value (Figure 2). The above results showed that the nomogram for predicting the prognosis in septic patients after gastrointestinal surgery could accurately predict the 90-d survival rate.

Internal validation of nomogram

We used the bootstrap method to internally verify the nomogram for predicting the prognosis in septic patients after gastrointestinal surgery. After 1000 internal verifications using the R software package and a repeated bootstrap self sampling method, the C-index was 0.876 (Supplementary Figure 2). This result was consistent

with the initial C-index of the nomogram, indicating that the nomogram had good discrimination.

Survival curve based on risk stratification

The total score was calculated according to the nomogram for predicting the prognosis of tumor patients with sepsis after gastrointestinal surgery, with a median of 233 points. According to the nomogram, 303 postoperative septic patients were divided into three subgroups: high-risk group (total score < 233), moderate-risk group (192 ≤ total score < 233), and low-risk group (total score ≥ 233).

The survival curves of postoperative septic patients are shown in Figure 3. The 90-d overall survival rates of postoperative septic patients in the high-risk group, moderate-risk group and low-risk group were 0.645, 0.883, and 0.989, respectively. There was a statistically significant difference in the 90-d survival rate among the three groups (P < 0.0001).

DISCUSSION

The nomogram was a graphical representation of complex mathematical formulas. Medical nomograms mainly use biological and clinical data to describe statistical prediction models. As a graphical statistical prediction model, a nomogram could provide clinicians with a personalized prediction to quantitatively evaluate the prognosis of patients. This study established an effective nomogram for the first time, that could accurately predict the 90-d survival rate of septic patients after gastrointestinal tumor surgery. The calibration curve showed that the nomogram was highly reliable. At the same time, we used the bootstrap method for internal verification, which showed that the prediction ability of the model was very good. In addition, the nomogram could divide individuals into high-risk, moderate-risk and low-risk groups, which indicated that it might be a good tool for predicting the prognosis of tumor patients with sepsis after gastrointestinal surgery.

The main purpose of analysing the prognostic factors of tumor patients with sepsis and establishing a prognostic prediction model was to identify high-risk patients with sepsis as soon as possible and improve the prognosis of these patients. At the same time, it also provided a reference for follow-up clinical research. How to quantify clinical features to achieve individualized prediction of prognosis in septic patients is still a great challenge. The nomogram listed each variable separately by graph and allocated a corresponding number of points for a given variable size. Then, the cumulative score of all variables was matched with the result scale to obtain the corresponding probability. Many studies have confirmed that the nomograms can predict the prognosis of clinical diseases[12-14]. Our study was also based on the nomogram established by the corresponding prognostic factors in septic patients, and we conducted internal validation.

Based on the nomogram for predicting the prognosis of the septic patients, the total score of patients could be calculated and patients could be divided into a high-risk group, moderate-risk group and low-risk group. According to the survival curve based on the nomogram to evaluate the prognosis of sepsis, we found a significant difference in the 90-d survival rate among the three groups, which might warn us to take early intervention in patients with sepsis. For an individual, we could score the patients according to the nomogram, and the corresponding scores could be preliminarily divided into risk groups, which could provide a basis for clinicians to explain the condition to patients and their families and reduce some doctor-patient contradictions and disputes. Of course, whether the nomogram could be widely popularized remains to be verified.

Sepsis was one of the most common causes of mortality in the ICU. Due to its complex etiology and high heterogeneity, there were great differences in the mortality reported in various studies. At present, only a few studies on sepsis have been aimed at postoperative patients with gastrointestinal tumor[15-17]. The object of the study was septic patients after gastrointestinal tumor surgery, and the mortality was lower than that of septic patients reported in some literature[2,18], which might be closely related to

the fact that most of the infection sources of septic patients in this study were abdominal infections that could be actively treated at an early stage by multidisciplinary cooperation in our hospital. In this study, 303 septic patients after gastrointestinal surgery were analysed retrospectively. Multiple survival analysis showed that there were statistically significant differences in tumor type, whether there was septic shock, number of lymphocytes after entering the ICU, serum creatinine and total operation times on the prognosis of these septic patients. Among these factors, except whether there was septic shock, which had a medium ability to predict the prognosis of these septic patients alone, the other factors had a low ability to predict the prognosis of these septic patients. The predictive ability of the nomogram established by combining the five factors was significantly higher than that of individual factors. In the following, we analysed some prognostic factors.

Data published in recent years by the National Cancer Center show that gastric cancer and colorectal cancer incidence rates were the second and third respectively[19]. It is well known that there are differences in the long-term survival rates between patients with gastric cancer and colorectal cancer. On the basis of the estimation of the World Health Organization's Global Cancer Observatory, the 1-year and 5-year survival rates of gastric cancer patients in the United Kingdom from 2010 to 2014 were 46.8% and 20.8% respectively; while in colorectal cancer they were 79.3% and 60% respectively[20]. However, there have been few studies on the prognostic difference between septic patients after gastric cancer surgery and septic patients after colorectal cancer surgery. A prospective, multicenter study in Finland showed that the inpatient mortality of sepsis after gastrointestinal surgery was 30.5%, but the study included fewer tumor patients and did not report the impact of tumor type on prognosis[16]. Our study was the first direct comparative analysis of the prognosis of septic patients after gastric cancer surgery and septic patients after colorectal cancer surgery. Because of the difference in prognosis between the two groups of septic patients, we considered that it was related to pathogenic microorganisms, the difficulty of infection source control and the stronger corrosiveness of digestive fluid in the upper gastrointestinal tract. In this

study, the stratified analysis revealed that the pathogenic microorganisms isolated from septic patients after gastric cancer surgery included 83 cases of G-bacilli, 43 cases of G + cocci and 21 cases of fungi; pathogenic microorganisms isolated from patients with postoperative sepsis of colorectal cancer included 106 cases of G-bacilli, 53 cases of G + cocci and 6 cases of fungi. There was a significant difference in the pathogens isolated from these two groups.

Patients with sepsis often experience severe immunosuppression and have a poor prognosis[21]. The immunosuppression of sepsis included innate and acquired immunosuppression. Human leukocyte antigen HLA-DR on the surface of monocytes, dendritic cell count and NK cell count were mainly used to monitor congenital immunosuppression in patients with sepsis, while acquired immunosuppression could be monitored by the number of lymphocytes. Studies have shown that the decrease in lymphocytes in patients with sepsis was an independent prognostic risk factor [22]. Other studies have shown that the prognosis of septic patients is related to the ratio of neutrophils and lymphocytes[23], and its essence is consistent with the number of lymphocytes. In our study, we also found that the decrease in the number of lymphocytes in septic patients after gastrointestinal surgery was associated with poor prognosis, but our study showed that the ratio of neutrophils to lymphocytes had no significant effect on the prognosis of septic patients, which might be related to the cut-off value in our study.

The kidney is one of the vulnerable organs in septic patients, and acute kidney injury (AKI) can even be as high as 50% in septic patients[24]. With the aggravation of sepsis, the probability of acute kidney injury increases accordingly[25]. The pathogenesis of acute kidney injury in sepsis is complex. Current evidence suggests that acute kidney injury might be functional rather than structural for at least the first 48 h. For example, septic AKI lacked histopathological changes but had microvascular abnormalities and tubular stress changes. In this case, renal medullary hypoxia caused by the redistribution of intrarenal perfusion was becoming a key factor in acute kidney injury in sepsis. Risk factors for acute kidney injury in septic patients included advanced age,

chronic renal insufficiency, diabetes, heart failure and cancer, *etc.* Septic patients complicated with acute kidney injury significantly worsen the prognosis[26,27]. At present, the diagnosis of sepsis related AKI followed the criteria of acute kidney injury issued by the global working group on improving the prognosis of kidney diseases (KDIGO) in 2012[28]. The treatment of AKI in sepsis mainly included volume resuscitation, antibiotics and renal replacement therapy. In our study, a serum creatinine level of 120 μmol/L was the cut-off value, and the patients were divided into two groups. There was a statistically significant difference in the 90-d survival rate between the two groups.

After gastrointestinal surgery, some patients with abdominal sepsis needed more than one operation to control the source of infection, which often suggested that the patient was in poor condition. The incidence of unplanned reoperation varies among hospitals due to the technical level of doctors[29]. As an important component of medical safety and quality management, unplanned reoperation is often used to assess the technical level of surgery. Therefore, we selected the number of operations to predict the prognosis of patients with sepsis. In our study, we found that there was a significant difference in the 90-d survival rate between septic patients after three operations and septic patients after one operation or two operations, although there was no statistically significant difference in the 90-d survival rate between septic patients after two operations and septic patients after only one operation. We considered that the mortality of patients with indirect operation-related infections (including pulmonary infection, urinary infection and central venous catheter-related infection) was higher than that of patients with direct operation-related infections (including thoracic and abdominal infection, intestinal infection, wound infection, skin and soft tissue infection and biliary tract infection). Among the patients who underwent only one operation, the proportion of indirect operation-related infections was higher. According to the stratified analysis of direct and indirect infections related to gastrointestinal surgery, the 90-d survival rate of patients in the group with two operations was slightly higher than that in the group with one operation, however the difference was not statistically

significant. This suggested that we might need more active surgical intervention for the treatment of sepsis caused by infection directly related to gastrointestinal tumor surgery. Of course, it needs to be verified by subsequent randomized controlled trials.

Some limitations of this study should be stated. First, this study was a single-center study, and the sample size was limited, so the results of this study might have some bias. Second, although the nomogram was established to predict the prognosis of these septic patients, it was not externally verified due to the limited sample size. Since there might be differences in patients with sepsis in different research centers, multicenter studies and external validation should be considered in the follow-up. Third, the population in our study was septic patients after gastrointestinal surgery in the ICU. Whether the results could be extended to all septic populations remains to be confirmed. Fourth, new biomarkers were not included in the prognostic factors selected in this study. These factors will be considered for further research to elaborate on the value of these new biomarkers. Fifth, this study spanned a long time, but since there was no significant difference in the 90-d survival rate of septic patients after gastrointestinal surgery before and after January 1, 2016, we believed that this study was highly feasible. Finally, with the progress of technology and treatment, the survival rate of patients with sepsis may be improved. Therefore, the accuracy of predicting prognosis by nomogram may be affected, which needs our attention.

CONCLUSION

The nomogram based on these five factors (tumor type, septic shock, number of lymphocytes, serum creatinine, and total operation times) could accurately predict the prognosis of tumor patients with sepsis after gastrointestinal surgery.

ARTICLE HIGHLIGHTS

Research background

There were few studies on the prognosis of tumor patients with sepsis after gastrointestinal surgery and there was no relevant nomogram for predicting the prognosis of these patients.

Research motivation

To explore the prognostic predictors in patients with sepsis after gastrointestinal tumor surgery.

Research objectives

The aim of the study was to establish a nomogram for predicting the prognosis of tumor patients with sepsis after gastrointestinal surgery in the intensive care unit (ICU).

Research methods

A total of 303 septic patients after gastrointestinal tumor surgery admitted to the ICU at Peking University Cancer Hospital from January 1, 2013 to December 31, 2020 were analysed retrospectively. The model for predicting the prognosis of these septic patients was established by the R software package.

Research results

The most common infection site of sepsis after gastrointestinal surgery in the ICU was abdominal infection. The 90-d all-cause mortality rate was 10.2% in our study group. In multiple analyses, we found that there were statistically significant differences in tumor type, septic shock, the number of lymphocytes after ICU admission, serum creatinine and total operation times among tumor patients with sepsis after gastrointestinal surgery ($P<0.05$). These five variables could be used to establish a nomogram for predicting the prognosis of these septic patients. The nomogram was verified, and the initial C-index was 0.861. After 1000 internal validations of the model, the C-index was 0.876, and the discrimination was good. The correction curve indicated that the actual value was in good agreement with the predicted value.

Research conclusions

The nomogram based on these five factors (tumor type, septic shock, number of lymphocytes, serum creatinine and total operation times) could accurately predict the prognosis of tumor patients with sepsis after gastrointestinal surgery.

Research perspectives

Need external validation in the future to verify the results.

Figure Legends

Figure 1 Nomogram for predicting the 90-d overall survival. Tumor type: 0 represents gastric cancer, 1 represents colorectal cancer, and 2 represents other abdominal tumors; Septic shock: 0 represents no, 1 represents yes; Number of lymphocytes: 0 represents ≤ 0.2×10^9/L, 1 represents > 0.2×10^9/L; Serum creatinine: 0 represents ≤ 120 μmol/L, 1 represents >120 μmol/L; Operation times: 1 represents 1 time, 2 represents 2 times, and 3 represents 3 times.

Figure 2 Calibration plot.

Figure 3 Kaplan-Meier estimate of the 90-d overall survival and risk assessment using the nomogram.

Table 1 Baseline characteristics of patients with sepsis

Baseline characteristics	Number (%)
Age, median (Q1, Q3)	66 (59,73)
Sex	
Male	235 (77.6)
Female	68 (22.4)
BMI, Mean (SD), kg/m^2	23.7 (4.0)
Tumor type	
Gastric cancer	138 (45.5)
Colorectal cancer	148 (48.8)
Other abdominal tumors	17 (5.6)
Coexisting disease[1]	
Hypertension	106 (35.0)
Diabetes	55 (18.2)
Coronary heart disease	32 (10.6)
Chronic obstructive pulmonary disease	15 (5.0)
Arrhythmia	22 (7.3)
Chronic renal insufficiency	4 (1.3)
Location of infection[2]	
Abdominal infection	229 (75.6)
Pneumonia	58 (19.1)
Intrathoracic infection	19 (6.3)
Enterogenous infection	16 (5.3)
Surgical wound infection	7 (2.3)
Skin and soft tissue infection	6 (2.0)
Central line-associated bloodstream infection	4 (1.3)
Urinary tract infection	4 (1.3)
Biliary infection	2 (0.7)
First surgery	
Laparoscopic	76 (25.1)
Open	227 (74.9)

[1]47 patients had more than one chronic disease.

[2]38 patients were infected with more than one site.

BMI: Body mass index.

Table 2 Univariate analysis of patients with sepsis

Parameters	Number (%)	Survival rate at 90-d	*P* value
Age, yr			0.405
≤ 65	149 (49.2)	0.913	
> 65	154 (50.8.0)	0.883	
Sex			0.190
Male	235 (77.6)	0.885	
Female	68 (22.4)	0.941	
BMI, kg/m2			0.013
≤ 20	59 (19.5)	0.797	
20 < BMI ≤ 30	225 (74.3)	0.924	
> 30	19 (6.3)	0.895	
Charlson score			0.298
≤ 3	229 (75.6)	0.908	
> 3	74 (24.4)	0.865	
Tumor type			0.026
Gastric cancer	138 (45.5)	0.848	
Colorectal cancer	148 (48.8)	0.946	
Other abdominal tumors	17 (5.6)	0.882	
The first operation was emergency			0.725
No	268 (88.4)	0.896	
Yes	35 (11.6)	0.914	
First surgery			0.575
Laparoscopic	76 (25.1)	0.882	

Open	227 (74.9)	0.903	
Length of first operation, min			0.526
≤ 240	220 (72.6)	0.905	
> 240	83 (27.4)	0.880	
Empirical anti infection evaluation			0.001
Sensitive	229 (75.6)	0.917	
Resistance	26 (8.6)	0.692	
No pathogen detected	48(17.1)	0.917	
Septic shock			0.001
No	184 (60.7)	0.978	
Yes	119 (39.3)	0.773	
Leukocyte count, 10^9/L			0.143
≤ 4	49 (16.2)	0.837	
4 < WBC ≤ 12	142 (46.9)	0.930	
> 12	112 (37.0)	0.884	
Number of lymphocytes, 10^9/L			0.004
≤ 0.2	28 (9.2)	0.750	
> 0.2	275 (90.8)	0.913	
Neutrophil to lymphocyte ratio			0.883
≤ 20	218 (71.9)	0.899	
> 20	85 (28.1)	0.894	
APTT, S			0.003
≤ 50	244 (80.5)	0.922	
> 50	59 (19.5)	0.797	
Albumin, g/L			0.279
≤ 30	168 (55.4)	0.881	
> 30	135 (44.6)	0.919	
Serum creatinine, umol/L			0.001
≤ 120	256 (84.5)	0.926	
> 120	47 (15.5)	0.745	

Cardiac troponin I, ng/mL			0.130
≤ 0.05	253 (83.5)	0.909	
> 0.05	50 (16.5)	0.840	
Procalcitonin, ng/mL			0.034
≤ 10	214 (70.6)	0.921	
> 10	89 (29.4)	0.843	
Lactic acid, mmol/L			0.001
≤ 3	227 (74.9)	0.934	
> 3	76 (25.1)	0.789	
Oxygenation index, mmHg			0.001
≤ 200	146 (48.2)	0.836	
> 200	157 (51.8)	0.955	
SOFA score			0.001
≤ 6	175 (57.8)	0.983	
> 6	128 (42.2)	0.781	
Gastrointestinal fistula or perforation			0.364
No	183 (60.4)	0.885	
Yes	120 (39.6)	0.917	
Operation times			0.001
1	174 (57.4)	0.885	
2	123 (40.6)	0.943	
3	6 (2.0)	0.333	

BMI: Body mass index; SOFA: Sequential organ failure score; APTT: Activated partial thromboplastin time.

3

Table 3 Multiple analysis of patients with sepsis

Factors	B	HR	95% interval		*P* value
			Lower	Upper	
Tumor type (Ref: Gastric cancer)					0.007
Colorectal cancer	-1.254	0.286	0.125	0.657	0.003
Other abdominal tumors	-0.249	0.780	0.180	3.370	0.739
Septic shock	2.204	7.569	2.539	22.557	0.001
Number of lymphocytes	-1.209	0.298	0.120	0.742	0.009
Serum creatinine	1.163	3.199	1.463	6.992	0.004
Operation times (Ref: 1)					0.006
2	-0.704	0.485	0.202	1.162	0.105
3	1.609	4998	1.613	15.490	0.005

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