Original Article

Risk factors for sepsis in patients with colorectal cancer complicated with gastrointestinal perforation and its impact on prognosis

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Background: Colorectal cancer is the most common gastrointestinal tumor. Gastrointestinal perforation is a common complication of colorectal cancer, resulting in peritonitis, abdominal abscess, and sepsis, and can eventually lead to death. The present study aimed to investigate the risk factors for sepsis in patients with colorectal cancer complicated with gastrointestinal perforation and its impact on prognosis.

Methods: From January 2016 to December 2017, 126 patients with colorectal cancer complicated with gastrointestinal perforation admitted to the Dazu Hospital of Chongqing Medical University were retrospectively and continuously collected. The patients were divided into a sepsis group (n=56) and a control group (n=70) according to whether they developed sepsis or not. The clinical characteristics of the two groups were analyzed, and multivariate logistic regression analysis was performed to explore the risk factors of sepsis in patients with colorectal cancer complicated with gastrointestinal perforation. Finally, the impact of sepsis on the prognosis of patients was analyzed.

Results: The multivariate logistic regression analysis showed that anemia, intestinal obstruction, preoperative chemotherapy, acidosis, and albumin <30 g/L were independent risk factors for sepsis in colorectal cancer patients complicated with gastrointestinal perforation (P<0.05). Albumin was valuable in predicting the absence of sepsis in colorectal cancer patients complicated with gastrointestinal perforation, and the area under the curve was 0.751 (95% confidence interval: 0.666–0.835). R4.0.3 statistical software was used to randomly divide the dataset into training and validation sets, with a sample size of 88 in the training set and 38 in the validation set. The areas under the receiver operating characteristic curves of the training and validation sets were 0.857 (95% confidence interval: 0.776–0.938) and 0.735 (95% confidence interval: 0.568–0.902), respectively. The Hosmer-Lemeshow Goodness-of-Fit Test was performed in the validation set; the chi-square value was 10.274 and the P value was 0.246, which indicated that the model had good confidence in predicting sepsis.

Conclusions: Patients with colorectal cancer complicated by gastrointestinal perforation have a high incidence of sepsis, which can lead to a poor prognosis. The model presented in this study can effectively identify patients with a high risk of sepsis.

Keywords: Colorectal cancer; gastrointestinal perforation; sepsis; risk factors; prognosis

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Introduction

The incidence of colorectal cancer ranks third among all malignant tumors (1), and some patients may also have gastrointestinal perforation (2,3). The most common site of gastrointestinal perforation is the sigmoid colon, which accounts for about 50%, followed by the ascending colon, descending colon, and rectum. Abdominal pain is a common clinical symptom of gastrointestinal perforation; since colorectal cancer is more common in middle-aged and elderly patients and the elderly are relatively insensitive to peritonitis symptoms, patients can have no peritonitis symptoms in the early stage of gastrointestinal perforation, resulting in delayed diagnosis and treatment. Therefore, severe abdominal infection and even sepsis may be found upon diagnosis of colorectal cancer (4). Colorectal perforation is a life-threatening acute abdomen, accounting for up to 20% of patient deaths after emergency surgery (5). At present, there is a paucity of studies exploring the risk factors for sepsis in colorectal cancer patients complicated with gastrointestinal perforation and its impact on prognosis, and thus, we designed this study. We present the following article in accordance with the TRIPOD reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-205/rc).

Methods

General information

From January 2016 to December 2017, 126 patients with colorectal cancer complicated with gastrointestinal perforation were collected retrospectively and continuously from the Dazu Hospital of Chongqing Medical University. The patients were divided into a sepsis group (n=56) and a control group (n=70) according to whether they developed sepsis or not.

Inclusion criteria: (I) colorectal cancer; (II) combined with digestive tract perforation; (III) age ≥18 years old; (IV) received treatment at the Dazu Hospital of Chongqing Medical University with complete clinical data. Exclusion Criteria: (I) Combined with other malignant tumors; (II) recurrent colorectal cancer; (III) insufficiency in important organs such as liver and kidney; (IV) combined with infection in other parts; (V) distant metastasis; (VI) lost to follow-up.

This retrospective clinical study was performed in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of Dazu Hospital of Chongqing Medical University (No. c2022-03-132). The requirement for informed consent was waived due to the retrospective nature of the study. The patient inclusion flowchart is shown in *Figure 1*.

Diagnostic criteria

(I) Colorectal cancer: All patients were diagnosed with colorectal cancer based on colonoscopy or postoperative pathological diagnosis. (II) Gastrointestinal perforation: Abdominal X-ray showed free gas in the abdomen, and colorectal perforation was confirmed during surgery. (III) Sepsis: Abdominal drainage fluid was retained, and bacterial culture confirmed the existence of abdominal infection. Moreover, if the sepsis-related sequential organ failure assessment score increased by ≥2 points from baseline, the patient was diagnosed with sepsis (6).

Treatment

All patients were given symptomatic supportive care, such as electrocardiogram monitoring, early fluid resuscitation, anti-infection, and maintenance of electrolyte balance after admission (6). At the same time, emergency surgery was performed. After surgery, symptomatic supportive therapy such as anti-infection treatment could be continued, and if necessary, organ function support therapy, such as mechanical ventilation and continuous hemofiltration, could also be given. After surgery, according to the pathological results, it was decided whether to administer chemotherapy.

Highlight box

Key findings

- Anemia, intestinal obstruction, preoperative chemotherapy, acidosis, and albumin <30 g/L are independent risk factors for sepsis in colorectal cancer patients complicated with gastrointestinal perforation.

What is known and what is new?

- Perforation of the digestive tract can lead to complex intra-abdominal infection, leading to peritonitis, intra-abdominal abscess, and progression to sepsis and septic shock.
- Colorectal cancer combined with gastrointestinal perforation can lead to poor prognosis, and this model can effectively identify patients at a high risk of sepsis.

What is the implication, and what should change now?

- Intervention through the timely identification of high-risk patients and associated risk factors may be beneficial in improving patient outcomes; however, further clinical studies are still needed.

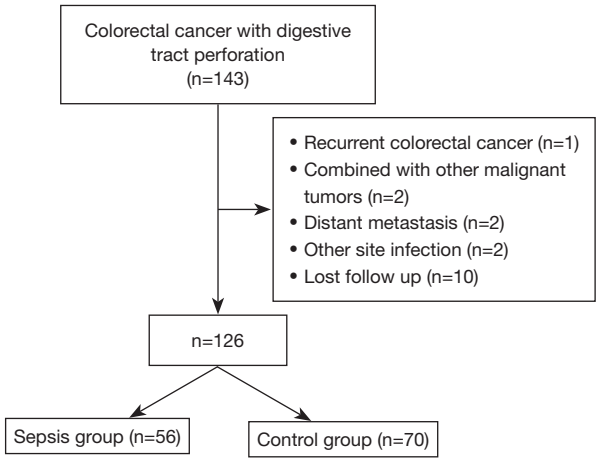

Figure 1 Patient inclusion flow chart.

The patients were followed up for 5 years, and the 5-year survival rate was observed.

Data collection

The following data were collected: age, sex, course of abdominal pain, body mass index, diabetes, hypertension, tumor location, tumor size, degree of tumor cell differentiation, tumor cell type, lymph node metastasis, peripheral invasion, vascular tumor thrombus, anemia, intestinal obstruction, preoperative chemotherapy, acidosis, and preoperative albumin.

Statistical analysis

SPSS26.0 (IBM, Armonk, NY, USA) was used to complete the data analysis, and P<0.05 indicated that the difference was statistically significant (two-tailed). The measurement data, such as age and tumor size, of the two groups were expressed by the mean ± standard deviation, and the differences between the two groups were analyzed by an independent sample *t*-test. The gender, diabetes status, and other counting data of the two groups were expressed by n (%), and the chi-square test was used to analyze the differences between the two groups.

Multivariate logistics regression analysis was used to explore the risk factors for sepsis in patients with colorectal cancer complicated with gastrointestinal perforation. The receiver operating characteristic (ROC) curve was used to analyze the predictive value of albumin in colorectal cancer patients complicated with gastrointestinal perforation. R4.0.3 statistical software was used to establish a sepsis prediction model in colorectal cancer patients complicated with gastrointestinal perforation.

Results

Comparison of the clinical features between the two groups

Compared with the control group, the proportion of patients with abdominal pain >8 h, anemia, intestinal obstruction, preoperative chemotherapy, acidosis, and preoperative albumin <30 g/L was significantly increased in the sepsis group (P<0.05) (*Table 1*).

Risk factor analysis of sepsis in colorectal cancer patients complicated with gastrointestinal perforation

Multivariate logistic regression analysis showed that anemia, intestinal obstruction, preoperative chemotherapy, acidosis, and albumin <30 g/L were independent risk factors for sepsis in colorectal cancer patients complicated with gastrointestinal perforation (P<0.05) (*Table 2*).

Predictive value of albumin in colorectal cancer patients complicated with gastrointestinal perforation

Albumin was valuable in predicting the absence of sepsis in colorectal cancer patients complicated with gastrointestinal perforation, and the area under the curve was 0.751 (95% confidence interval: 0.666–0.835) (*Figure 2*).

Establishment and validation of a sepsis prediction model in colorectal cancer patients complicated with gastrointestinal perforation

R4.0.3 statistical software was used for statistical analysis. The dataset was randomly divided into a training set and a validation set, with a sample size of 88 in the training set and 38 in the validation set. Anemia, intestinal obstruction, preoperative chemotherapy, acidosis, and albumin were included in the predictive model. A nomogram and ROC curve were established, and the areas under the ROC curves in the training and verification sets were 0.857 (95% confidence interval: 0.776–0.938) and 0.735 (95% confidence interval: 0.568–0.902), respectively. In the validation set, the model was tested with Hosmer-Lemeshow Goodness-of-Fit, with a chi-square value of 10.274 and a P value of 0.246 (*Figures 3*,*4*).

Table 1 Comparison of clinical features between the two groups

Variables	Sepsis group (n=56)	Control group (n=70)	t/χ^2 value	P value
Age (years), mean ± standard deviation	61.63±9.08	63.63±8.90	1.245	0.216
Gender, n (%)			0.000	1.000
Male	32 (57.14)	40 (57.14)		
Female	24 (42.86)	30 (42.86)		
Abdominal pain course (h), mean ± standard deviation	17.05±6.90	12.67±5.90	3.842	0.000
Duration of abdominal pain >8 h, n (%)	47 (83.93)	47 (67.14)	4.627	0.031
Body mass index (kg/m^2), mean ± standard deviation	24.06±2.58	23.94±2.33	0.309	0.758
Diabetes, n (%)	6 (10.71)	8 (11.43)	0.016	0.899
Hypertension, n (%)	9 (16.07)	15 (21.43)	0.579	0.447
Location of the tumor, n (%)			2.308	0.129
Colon	43 (76.79)	40 (57.14)		
Rectum	13 (23.21)	30 (42.86)		
Tumor size (cm), mean ± standard deviation	6.21±1.86	6.24±1.84	0.083	0.934
The degree of differentiation, n (%)			0.838	0.360
Low or undifferentiated	12 (21.43)	20 (28.57)		
Medium to high differentiation	44 (78.57)	50 (71.43)		
Tumor cell type, n (%)			0.041	0.839
Adenocarcinoma	51 (91.07)	63 (90.00)		
Non-adenocarcinoma	5 (8.93)	7 (10.00)		
Lymph node metastases, n (%)			0.250	0.617
Yes	46 (82.14)	55 (78.57)		
No	10 (17.86)	15 (21.43)		
Peripheral invasion, n (%)			0.295	0.587
Yes	21 (37.50)	23 (32.86)		
No	35 (62.50)	47 (67.14)		
Vascular tumor thrombus, n (%)			0.188	0.664
Yes	18 (32.14)	20 (28.57)		
No	38 (67.86)	50 (71.43)		
Anemia, n (%)			4.599	0.032
Yes	29 (51.79)	23 (32.86)		
No	27 (48.21)	47 (67.14)		
Ileus, n (%)			7.431	0.006
Yes	15 (26.79)	6 (8.57)		
No	41 (73.21)	64 (91.43)		

Table 1 *(continued)*

Table 1 *(continued)*

Variables	Sepsis group (n=56)	Control group (n=70)	t/χ^2 value	P value
Preoperative chemotherapy, n (%)			6.930	0.008
Yes	12 (21.43)	4 (5.71)		
No	44 (78.57)	66 (94.29)		
Acidosis, n (%)			16.665	0.000
Yes	42 (75.00)	27 (38.57)		
No	14 (25.00)	43 (61.43)		
Preoperative albumin (g/L), mean ± standard deviation	26.80±4.68	31.24±4.55	5.369	0.000
Preoperative albumin <30 g/L, n (%)	39 (69.64)	24 (34.29)	15.557	0.000

Table 2 Risk factors of sepsis in colorectal cancer patients complicated with gastrointestinal perforation

Variables	B-value	Standard error	Wald value	P value	Relative risk (95% CI)
Duration of abdominal pain >8 h	0.724	0.518	1.953	0.162	2.064 (0.747–5.700)
Anemia	0.955	0.448	4.539	0.033	2.598 (1.079–6.255)
Ileus	1.370	0.647	4.479	0.034	3.935 (1.107–13.995)
Preoperative chemotherapy	1.858	0.762	5.940	0.015	6.414 (1.439–28.584)
Acidosis	1.492	0.479	9.722	0.002	4.447 (1.741–11.360)
Albumin <30 g/L	0.939	0.451	4.330	0.037	2.558 (1.056–6.197)
Constant	–11.732	2.563	20.945	0.000	0.000

CI, confidence interval.

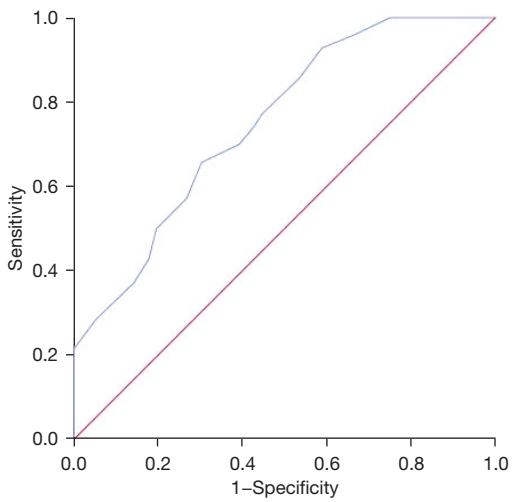

Figure 2 Predictive value of albumin in colorectal cancer patients complicated with gastrointestinal perforation.

Prognosis of colorectal cancer patients complicated with gastrointestinal perforation

Compared with the control group, the 5-year survival rate of patients in the sepsis group was significantly reduced (35.71% *vs.* 57.14%, P=0.017).

Discussion

Colorectal cancer combined with gastrointestinal perforation is a clinically common, yet critical and fatal disease. If the infection is not controlled in time, it can develop into sepsis, multiple organ failure, and eventually lead to death. It was confirmed by previous studies that postoperative infection after colorectal surgery have been associated with negative economic impact, increased morbidity, extended postoperative hospital stay, readmission,

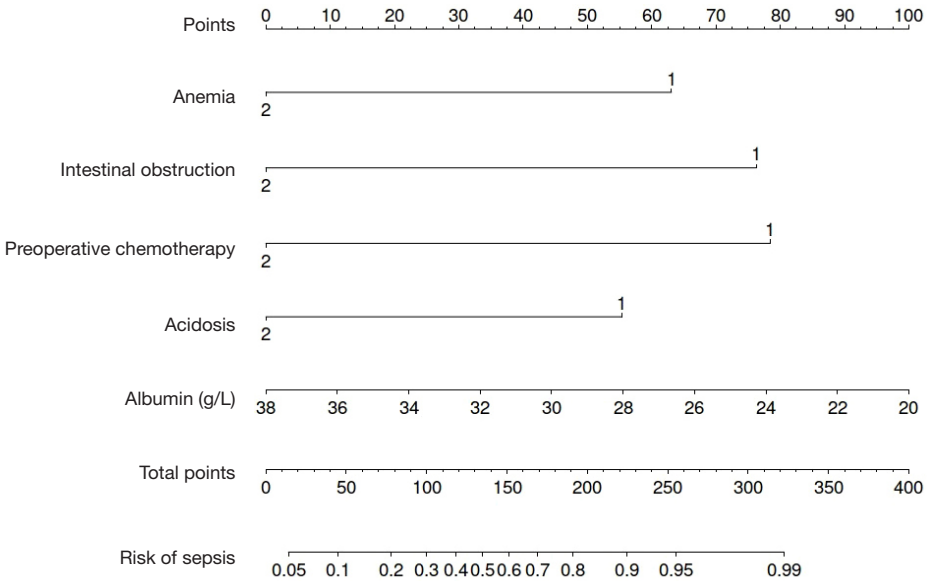

Figure 3 Nomogram of a sepsis prediction model in colorectal cancer patients complicated with gastrointestinal perforation.

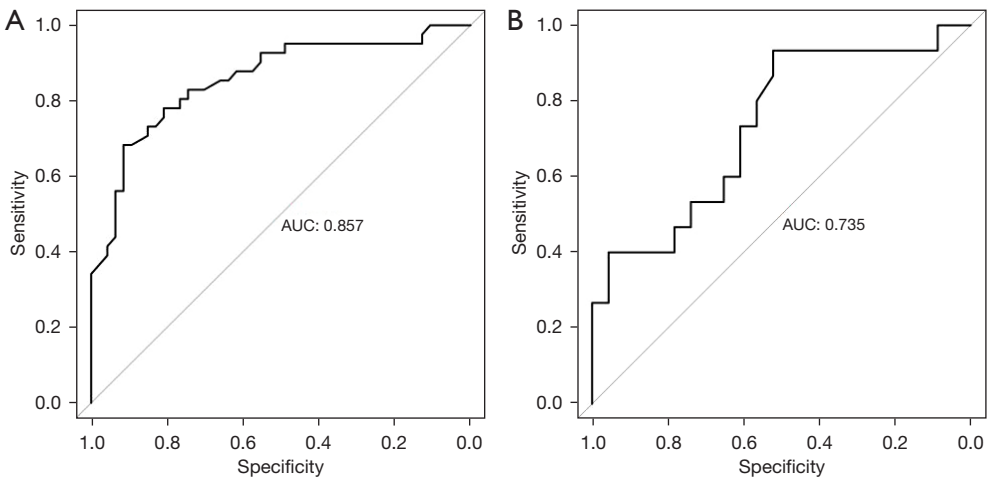

Figure 4 The value of the predictive model in predicting the sepsis in colorectal cancer patients complicated with gastrointestinal perforation. AUC, area under the curve.

sepsis, and death (7,8). Therefore, it is crucial to identify colorectal cancer patients complicated with gastrointestinal perforation who are at a high risk of sepsis. We designed the present study, which showed that anemia, intestinal obstruction, preoperative chemotherapy, acidosis, and albumin <30 g/L were independent risk factors for sepsis in colorectal cancer patients complicated with gastrointestinal perforation (P<0.05). The model established in the present study was valuable in predicting sepsis in colorectal cancer patients complicated with gastrointestinal perforation, with an area under the ROC curve of 0.857 (95% confidence interval: 0.776–0.938).

Digestive tract tumors can cause anemia in several ways: (I) Secretion of cytokines inhibits hematopoietic function; (II) digestive tract tumors lead to malnutrition, resulting in a serious lack of vitamins, iron, folic acid, and other hematopoietic raw materials; and (III) trans-gastrointestinal bleeding. Therefore, it is more common for colorectal cancer patients to have anemia, especially in patients with colorectal cancer in the middle and advanced

stages (9-12). Patients with anemia have decreased immune function and are prone to sepsis (13-15). If colorectal cancer grows into the intestinal lumen, it can cause intestinal obstruction. Intestinal edema will occur in patients with intestinal obstruction, resulting in an increase in intestinal permeability, water-electrolyte disturbance, and intestinal flora displacement, leading to sepsis (16). Intestinal permeability is increased in patients with preoperative chemotherapy, and intestinal edema is obvious in some patients. Moreover, chemotherapy can suppress the body's immunity, resulting in the spread of infection (17). Acidosis refers to the accumulation of acidic substances in the blood and tissues in the body, while its essence is the increased concentration of hydrogen ions in the blood. Acidosis includes respiratory acidosis and metabolic acidosis; it is the embodiment of tissue ischemia and hypoxia, indicating insufficient tissue perfusion. If acidosis is not corrected in time, it can promote the progression of sepsis (18,19). Albumin has numerous biological functions in patients with infection: (I) Maintenance of hemodynamic stability and reduction of tissue edema; and (II) it is an important protein involved in the body's immunity. When albumin is reduced, its effect is limited, so patients become prone to sepsis. Albumin should be supplemented in time in gastrointestinal perforation patients with a low albumin level (20-23). Finally, according to the literature, following colorectal cancer procedures, postoperative sepsis is significantly more common among patients over 65 years old, ASA score >2 (7). However, no similar results were observed in the present study, which may be due to the fact that only patients with gastrointestinal perforation were included in this study.

In addition, to more efficiently identify people at high risk of sepsis, we built a nomogram predictive model. The results showed that this model was valuable in predicting sepsis in colorectal cancer patients complicated with gastrointestinal perforation. The prognoses of many diseases are multifactorial, and thus, the prognostic value of using a single factor to predict patients is limited (24-27). In recent years, some scholars have pointed out that a nomogram prediction model can be built to synthesize multiple biological indicators, which can more effectively predict the prognosis of patients, and the value of this model has been confirmed in patients with sepsis (28-32).

Limitations

This was a retrospective clinical study, and the incidence of gastrointestinal perforation was relatively low due to the popularity of colonoscopy, etc. Therefore, the total number of cases included in this study was relatively insufficient.

Conclusions

Colorectal cancer patients complicated with gastrointestinal perforation have a high incidence of sepsis, which can lead to a poor prognosis. The model presented in this study can effectively identify patients at a high risk of sepsis. Intervention through timely identification of high-risk patients and risk factors may be beneficial in improving patient outcomes; however, further clinical studies are still needed.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-205/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-205/dss

Peer Review File: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-205/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-23-205/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective clinical study was performed in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of Dazu Hospital of Chongqing Medical University (No. c2022-03-132). The requirement for informed consent was waived due to the retrospective nature of the study.

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