Risk factors for developing high-output ileostomy: a retrospective study

Xiao Jian'an (✉ xiaojawsk@126.com)

Anyang Tumor Hospital <https://orcid.org/0000-0003-3126-1492>

Dongxiao Bai

Anyang Tumor Hospital

Lei Li

Anyang Tumor Hospital

Zhiling Shen

Anyang Tumor Hospital

Tianchen Huang

Anyang Tumor Hospital

Qingbing Wang

Anyang Tumor Hospital

Yanjun Wang

Anyang Tumor Hospital

Yong Zhang

Anyang Tumor Hospital

Zhipeng Guo

Anyang Tumor Hospital

Kan Li

Anyang Tumor Hospital

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Abstract

Background Prophylactic ileostomy and colostomy have been widely used to reduce the risk and complications of anastomotic leakage with high-risk colorectal cancer after operation. However, prophylactic ileostomy itself has some complications, and ileostomy high out-put syndrome is one of them. This study was performed to explore the risk factors of HOS in ileostomy.

Methods A total of 114 patients with HOS were screened out from 494 eligible ileostomy patients in the last five years. The clinical and pathological data were analyzed. The relationship between HOS and clinicopathological data was analyzed. Multivariate analysis was performed by logistic regression.

Results There was no clear correlation between the occurrence of HOS with sex, age, gross typing, histological grade, location of tumors, lymph node metastasis and TNM stage ($p>0.05$). Preoperative complications including inflammatory bowel disease, diabetes mellitus and neoadjuvant chemoradiotherapy were risk factors for HOS ($p<0.05$). Total colectomy and abdominal infection were risk factors for HOS ($p<0.05$) during operation.

Conclusion Inflammatory bowel disease, diabetes mellitus and neoadjuvant radiotherapy and chemotherapy in patients with colorectal cancer are the preoperative risk factors for HOS. Total colectomy and postoperative abdominal infection are the postoperative risk factors for HOS.

Background

Among Chinese, Colorectal cancer (CRC) is the fourth most common tumor in men and the third in women. This accounts for 10.46% of all new cancer cases in men and 9.17% in women. Furthermore, the incidence of colorectal cancer is increasing [1]. Fortunately, more standardized and individualized treatments have reduced the mortality and improved the quality of life of CRC patients. Clinically, prophylactic ileostomy and colostomy have been widely used to reduce the risk and complications of anastomotic leakage with high-risk colorectal cancer after operation [2, 3].

In general the indications of ileostomy include colon injury, colorectal cancer, familial polyposis, ulcerative colitis, Crohn's disease, etc. Patients who are suffering severe colon lesions cannot be resected permanently or temporarily. To relieve the intestinal obstruction patients may also undergo permanent or temporary ileostomy. For middle and low rectal cancer [4] as well as left colon cancer with obstruction, edema or others with high-risk factors, it may be necessary to adopt preventive ileostomy to reduce the risk and complications of anastomotic leakage when resecting the lesion and one-stage anastomosis. However, prophylactic ileostomy itself has some complications, and ileostomy high out-put syndrome is one of them.

The risk factors and predictors of high-output ileostomy have been reported in studies with a small sample size [5, 6]. We conducted a single-institution retrospective review of CRC. Patients underwent

ileostomy in our hospital, and were analyzed with clinical and pathological data to explore the risk factors of high-output ileostomy.

Methods

Ileostomy (both prophylactic and therapeutic) was performed in CRC patients between 2013 to 2018 in Anyang Tumor Hospital of Henan province China. HOS was defined as patients whose daily stoma output is more than 2000 ml and lasted more than two days as previous study reported [7]. Patients enrolled were between the age of 26 to 87 years old, with complete medical records and were followed up either with ileostomy reversal or more than one year after ileostomy. The others were excluded from the group whose stoma discharge was not detailed and did not meet the follow-up requirements. There were 114 patients (63 males and 51 females) with HOS were screened out from 494 eligible ileostomy patients in last five years.

Early HOS (EHOS) was defined as HOS developed within 3 weeks after operation, and late HOS (LHOS) was those over 3 weeks.

We collected clinical data using patient medical records, outpatient follow-ups, pathological stages, and complications like stoma discharge, electrolyte imbalance, dehydration, as well as disease treatments. Discharged patients were followed up to 1 year after ileostomy or ileostomy reversal.

SPSS17.0 statistical software was used for the statistical analysis. Single factor analysis was performed using chi-square test and Fisher's exact probability method. Multifactor analysis was performed with logistic regression. $P<0.05$ had statistical significance.

Results

1. Common symptoms of HOS.

Dehydration was the most common symptom of HOS (37.7%), followed by electrolyte disturbance (28.1%), local dermatitis (21.9%), renal dysfunction (5.3%) and malnutrition (7.0%) in long-term HOS (Table 1).

Table 1		
Composition Ratio of Common Symptoms of HOS.		
HOS	(n=114)	Proportion(%)
Dehydration	43	37.7
Electrolyte disturbance	32	28.1
Hyponatremia	21	18.4
Hypochloritemia	18	15.8
Hypokalemia	14	12.3
Hypomagnesemia	4	3.5
Renal dysfunction	6	5.3
Malnutrition	8	7.0
Local dermatitis	25	21.9

2. Correlation between HOS and clinicopathological features of CRC.

The results showed that there is no clear correlation between the occurrence of HOS with gender, age, gross typing, histological grading, tumor location, lymph node metastasis and TNM staging in patients with colorectal cancer (Table 2).

Table 2
Relationship between HOS and clinical-pathological features.

Clinicopathological	Cases	Indicators HOS n(%)	P value
Gender			0.741
male	271	61 (22.5)	
female	223	53 (23.8)	
Age			0.537
>60 years old	193	44 (22.8)	
≤ 60 years old	291	70 (24.1)	
Gross type			0.726
massive type	219	53(24.2)	
Ulcerative type	162	38(23.5)	
Infiltrating type	113	23(20.4)	
Organizational grading			0.197
Highly differentiated	178	36(20.2)	
Medium differentiation	191	42(22.0)	
poorly differentiated	125	36(28.8)	
Tumor site			0.487
rectum	351	79(22.5)	
colon	143	35(24.5)	
Lymph node metastasis			0.487
Yes	307	74(24.1)	
No	187	40(21.4)	
TNM staging			0.934
Phase I	55	13(23.6)	
Phase II	85	20(23.5)	
Phase III	229	50(21.8)	
Phase IV	125	31(24.8)	

3. HOS and preoperative complications.

These data showed that preoperative complications of inflammatory bowel disease, diabetes mellitus and neoadjuvant chemoradiotherapy are associated with the occurrence of HOS in patients with colorectal cancer (Table 3).

Table 3

Univariate analysis of preoperative complications in HOS and non-HOS groups.

Complications	Ileostomy n(%)		P value
	HOS(n = 114)	Non-HOS(n = 380)	
Inflammatory bowel disease	14(12.3)	4 (1.1)	0.00*
Diabetes	18(15.8)	10(2.6)	0.00*
Mental disorder (tension)	5(4.4)	15(3.9)	0.84
intestinal obstruction	6(5.3)	21(5.5)	0.91
Hypoproteinemia	11(9.6)	42(11.1)	0.96
Anemia	6(5.3)	22(5.8)	0.83
Neoadjuvant chemoradiotherapy	23(20.2)	49(12.9)	0.04*
Steroid hormones	4(3.5)	6(1.6)	0.18
* The difference was statistically significant.			

4. HOS and surgical related indicators.

These figures showed that total colectomy and postoperative abdominal infection are correlated with the occurrence of HOS, but not with operation time, bleeding volume, application of diuretics and laparoscopy (Table 4).

Table 4

Univariate analysis of surgical related indicators in HOS and non-HOS groups.

Clinicopathological indicators	Ileostomy n(%)		P value
	HOS(n=114)	non-HOS(n=380)	
Radical operation			0.00*
Radical resection of rectal cancer	67(58.8)	250(65.8)	
Radical resection of colon cancer	34(29.8)	126(33.2)	
Total colectomy	13(11.4)	4(1.1)	
Laparoscopic surgery			0.467
Yes	81(71.1)	283(74.5)	
No	33(28.9)	97(25.5)	
Operative time			0.352
≥3h	61(53.5)	222(58.4)	
<3h	53(46.5)	158(41.6)	
Surgical bleeding volume			0.514
≥300ml	38(33.3)	115(30.3)	
<300ml	76(66.7)	265(69.7)	
Postoperative abdominal infection	8(7.0)	5(1.3)	0.00*
Postoperative application of Diuretics	3(2.6)	4(1.1)	0.204

* The difference was statistically significant.

5. EHOS/LHOS and related pathological factors.

The study demonstrated there is no significant difference between the occurrence of HOS and related pathological factors (inflammatory bowel disease, diabetes, mellitus, hypoproteinemia, neoadjuvant chemotherapy, anemia, etc.) in ileostomy patients (table 5).

Table 5

The relationship between EHOS, LHOS and related pathological factors.

Clinicopathological factors	HOS(n=114)n(%)		P value
	EHOS(n=69)	LHOS(n=45)	
Inflammatory bowel disease	10(14.5)	4 (8.9)	0.279
Diabetes	11(15.9)	7(15.6)	0.956
Mental disorder (tension)	3(4.3)	2(4.4)	1.000
Hypoproteinemia	8(11.6)	3(6.7)	0.520
Anemia	4(5.8)	2(4.4)	1.000
Neoadjuvant chemoradiotherapy	11(15.9)	12(26.7)	0.163
Steroid hormones	3(4.3)	1(2.2)	0.483

6. Multivariate Analysis of Related Factors with HOS.

The indicators related to the occurrence of HOS in univariate analysis were further analyzed by multivariate analysis. This study showed that preoperative complications including inflammatory bowel disease, diabetes mellitus, neoadjuvant chemoradiotherapy, total colectomy and postoperative abdominal infection were risk factors of HOS ($P < 0.05$) (table 6).

Table 6

Logistic regression multivariate analysis.

Clinicopathological factors	B	S.E	Wals	Sig.	Exp (B)	95%CI
Inflammatory bowel disease	3.517	.636	30.555	.000	33.686	9.680-117.229
Diabetes	3.061	.508	36.244	.000	21.351	7.882-57.841
Neoadjuvant hemoradiotherapy	2.149	.425	25.533	.000	8.580	3.727-19.749
Total colectomy	1.191	.354	11.344	.000	3.291	1.646-6.584
Steroid hormones	3.470	.701	24.472	.000	32.146	8.133-127.060

Conclusion

These results indicate that inflammatory bowel disease, diabetes mellitus and neoadjuvant chemoradiotherapy are preoperative risk factors for HOS in CRC patients. Total colectomy and postoperative abdominal infection are the postoperative risk factors for HOS.

Discussion

HOSs or high-output syndrome is rarely studied and lacks attention. There is no consensus on the definition of HOSs (HOS) [5,7,8,9,10]. Dehydration, electrolyte disturbance (hyponatremia, hypochloremia, hypomagnesemia), renal failure and malnutrition (late stage) can occur in high-output ileostomy [5,7,8]. HOS increases the risk of readmission of CRC patients. Some scholars defined HOS as stoma output of more than 1500ml per day for more than two consecutive days [8, 9], while the others advocate that HOS should be defined as the output of more than 2,000 ml per day for more than two or three consecutive days [5,7]. As the complications are more likely to occur when the daily stoma output exceeds 2000mL, we adopt the latter standard in our study. HOS can be classified as early (<3 weeks after initial ostomy surgery) or late HOS (3 weeks after surgery) and this is widely accepted by previous studies.

In our cohort, the incidence of HOSs (114/494) was 23.07%, higher than earlier reports (17%)[7]. Dehydration was the most common symptom of HOS (37.7%), followed by electrolyte disturbance (28.1%), local dermatitis (21.9%), renal dysfunction (5.3%) and malnutrition (7.0%) in long-term HOS. It was reported that the incidence of HOS is 26% in 262 patients with ileostomy during hospitalization, 30% of patients were re-admitted within 30 days after discharge, and 37% of patients with re-hospitalization were due to dehydration [11]. The re-admission risk of ileostomy patients with inflammatory bowel disease was double that of other risk factors (OR 2.04) [12].

Among the related factors of operation, total colectomy and abdominal infection are the risk factors of HOS, but not the operation time, bleeding volume, diuretic application and laparoscopic operation. Diabetes mellitus and total colectomy are high risk factors for HOS, which are consistent with previous study [5]. As it is reported bile acid deficiency is one of the mechanism of total colectomy caused HOS. Total proctocolectomy prevents the reabsorption of bile acids absorbed by the ileocecum, as a result decrease in bile acid pools inhibits lipid absorption. Consequently, unabsorbed long-chain fatty acids are hydroxylated or desaturated by anaerobic intestinal bacteria, triggering the secretion of fluid and electrolytes, which may lead to the development of HOS [5]. Bile acid deficiency may also cause changes in the intestinal flora that increase intestinal drainage [15]. The loss of water absorption by the colon in

patients undergoing total colectomy can also lead to high ileostomy output. In our study, we did not find that the use of steroids and diuretics after ileostomy increase the high output of ileostomy, but the use of large doses of diuretics may increase the risk of dehydration.

Generally, half of the EHOS patients required no special drug intervention until recuperation, while the other half required drug intervention [7]. For the treatment and management of HOS, patients should be managed and guided throughout the hospital and after discharge [16]. In addition to basic treatments (such as restricting fluid intake, rehydration and correcting electrolyte disturbance) reducing the secretion of somatostatin and oral intake of loperamide is also effective in reducing discharge. Pieter-Jan Cuyle reported that 17% of patients with ileostomy had high excretion [17]. This complication would affect the implementation or completion of adjuvant therapy. Somatostatin analogues (ranitides, etc.) could reduce the excretion of ileostomy effectively. Routine dosage of loperamide is 20 mg twice daily by mouth, but dosage can be increased if not effective. Alicia Mackowski reported that increasing the dosage of loperamide to 300 mg per day in individual patients can reduce the amount of stoma excretion, without observed abnormality in renal function [18].

This paper is a retrospective study with some limitations. Prospective study should pay attention to the patients with high risk factors HOS, strengthen the supervision and treatment after operation and discharge for reducing the complications of stoma, and facilitate the smooth progress of comprehensive treatment as well as the re-admission rate caused by HOS [19-22].

We followed up with patients who had ileostomy reversal or 1 year after ileostomy by inpatient medical records, outpatient review and telephone follow-up. These data mostly came from patients' observation records in the hospital (including outpatient review) belonging to on-site data collection. Using remote video conference to evaluate ileostomy output, and taking early intervention measures to improve prognosis is a method worth exploring [23]. Multicenter, large sample randomized controlled studies of HOS should be conducted in the future.

Abbreviations

Colorectal cancer: CRC

High-output stoma: HOS

Early High-output stoma: EHOS

Late High-output stoma: LHOS

Declarations

Ethics approval and consent to participate

The study protocol was approved by the ethical committee for scientific research and drug clinical trial of AnYang Tumor Hospital (NO. AZLL022019048190812).

Consent for publication

Not applicable

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author information

Dongxiao Bai and Lei Li contributed equally to this work.

Affiliations Department of Surgery, Anyang Tumor Hospital, HeNan Province, China. Address: No. 1 Huanbin North Road, Anyang, Henan Province, China 455000.

Contributions J.A.X ,D.X.B..and L.L designed the study. Z.L.S, T.C.H and Y.Z collected clinical data. Q.B.W,L.L and Y.J.W. performed the statistical analysis. D.X.B and L.L. wrote the manuscript, J.A.X. reviewed and revised. All authors approved the final version of the manuscript.

Corresponding author Correspondence to Jian'an Xiao.

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