Organ/space infection is a common cause of high output stoma and outlet obstruction

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Abstract

Aim: The objectives of this study are to identify causes of high-output stoma (HOS) and outlet obstruction (OO), which are major complications of diverting ileostomy.

Methods: A retrospective analysis was performed in 103 patients who underwent colorectal surgery and diverting ileostomy between December 2015 and November 2018.

Results: HOS was found in 32 patients (31.1%) and OO in 19 (18.4%). Organ/space surgical site infection (SSI), anastomotic leakage and OO were independent HOS-related factors in univariate analysis, and OO (odds ratio [OR] 3.82, $p=0.022$) was a independent HOS-related factor in multivariate analysis.

Organ/space SSI and HOS were independent OO-related factors in univariate analysis, and organ/space SSI (OR 3.69, $p=0.02$) was a independent OO-related factor in multivariate analysis. The white blood cell (WBC) count on postoperative day (POD) 3 was significantly higher in the HOS group compared to the non-HOS group (9765 vs. 8130 /mL, $p<0.05$), and the WBC count (9400 vs. 7475 /mL, $p<0.05$) and C-reactive protein level (6.01 vs. 2.92 mg/L, $p<0.05$) on POD 6 were significantly higher in the OO group compared to the non-OO group.

Conclusion: Organ/space infection is involved in the common pathology of HOS and OO. Decreased intestinal absorption due to intestinal edema caused by organ/space SSI and relative stenosis at the abdominal wall-penetrating site are major causes of HOS and OO

Background

Diverting ileostomy reduces the risk of anastomotic leakage (AL) after surgery for rectal cancer, and use of diverting stoma (DS) has increased [1–3]. However, complications of ileostomy-related high output stoma (HOS) and outlet obstruction (OO) have incidences of 16–23%^{4, 5} and 5.6–25.8% [4, 5], respectively. HOS cause dehydration, electrolyte imbalance and renal dysfunction, resulting in a significant decrease of QOL. Most studies of HOS have described detection or management, but few have examined the pathology of HOS. Causes of HOS include diabetes, total proctocolectomy, intraabdominal abscess, paralytic ileus, AL and OO, but no clear pathology has been shown [6–11]. OO is defined as intestinal obstruction in an abdominal wall-penetrating site, but differs from general intestinal obstruction because symptoms are relieved by tube insertion from the stoma. Causes of OO include total proctocolectomy and the thickness of the rectus abdominis muscle, but as for HOS, the pathology remains to be elucidated [12–14]. Furthermore, no study has examined HOS and OO simultaneously and the relationship between HOS and OO is unknown. Therefore, this study was performed as a retrospective examination of patients with DS to determine the pathology and relationship of HOS and OO, and to identify related factors.

Methods

The subjects were 103 consecutive patients who underwent colorectal surgery and DS between December 2015 and November 2018. The study was performed as a retrospective analysis. The indications for DS creation were intersphincteric resection (ISR), preoperative therapy, or male patients with anastomosis just above anal canal after total mesorectal excision. Patients who underwent total proctocolectomy or emergency surgery were often considered for DS creation. The DS site was 40 cm distant from the terminal ileum in the right lower abdomen to penetrate the abdominal wall in the direction to allow lifting of the wall naturally. The aponeurosis of the rectus abdominis muscle was longitudinally incised with a two-finger width. A standardized technique was used to create the loop stoma.

Patient characteristics of age, sex, disease, body mass index (BMI), diabetes, smoking history, preoperative blood albumin (Alb), preoperative estimated glomerular filtration rate (eGFR) and thickness of the rectus abdominis muscle were examined. The thickness of the rectus abdominis muscle was measured using a slice at the umbilical level on CT recorded immediately before surgery. A straight line was drawn orthogonally to the horizontal axis at the maximal thickness, and the thickness of the rectus abdominis muscle was determined [13]. Surgical factors, such as operative procedure, approach, lateral lymph node dissection (LLND), operative time, blood loss volume, transfusion, intraoperative fluid, anastomotic procedure were also examined. The preoperative conditions including perforation, stenosis and preoperative chemotherapy were also examined.

Postoperative complications were analyzed using the Clavien-Dindo classification. AL was defined as clinical symptoms such as fever, abdominal pain and peritoneal irritation, and based on pus-like or stool-like output draining from the pelvic floor, anastomotic dehiscence found in a digital rectal examination, extravasation of endoluminally administered water-soluble contrast enema, and fluid or gas retention surrounding the anastomotic site detected by CT. Organ/space surgical site infection (SSI) was defined as antibiotic therapy for fever, abdominal pain and peritoneal irritation without marked findings of AL.

HOS was defined as two-days continuous output of >1500 mL per day [15]. OO was defined as symptoms of intestinal obstruction, imaging of caliber changes in the abdominal wall-penetrating site in ileostomy by CT, and a condition that was improved by tube retention in the oral stoma [14, 16]. These symptoms and signs were used to confirm the diagnosis of OO. Associations of clinical factors with HOS and OO were examined by Fisher chi-square test and Mann-Whitney U test. Factors with a significant difference ($p < 0.05$) were then evaluated by multivariate analysis. All statistical analyses were conducted using EZR [17].

Results

Background of subjects

The median age of the 103 patients was 66 years-old and the median BMI was 22.9 (16.9–38.9) kg/m². Eighty two (80%) patients were male, 16 (15.5%) patients had diabetes, 26 (25.2%) were smokers, and 6 (5.8%) were being treated with steroids. Preoperatively, the Alb level was 4.2 (2.4–5.0) g/dL, eGFR was

74.9 (20.1–135.2) mL/min/1.73 m², and the thickness of the rectus abdominis muscle was 10.25 (5.46–19.14) mm. The underlying diseases were malignant tumor in 84 (81.2%) patients, inflammatory bowel disease in 17 (16.5%), and perforation of colon in 2 (1.9%).

Surgical procedures were low anterior resection in 52 (50.5%) patients, intersphincteric resection in 31 (30.1%), total proctocolectomy in 17 (16.5%), and high anterior resection, sigmoidectomy and ileocecal resection in one subject each. Anastomotic procedures were a double stapling technique in 57 (55.3%) patients and hand-sewn anastomosis in 46 (44.7%). Approaches for intraperitoneal cavity used laparoscopy in 78 (75.7%) patients, a robot-assisted method in 15 (14.6%), and laparotomy in 10 (9.7%). LLND was performed in 28 (27.2%) patients and preoperative chemotherapy in 34 (33%). The median operative time was 319 (123–639) min, median blood loss volume was 60 (0–3550) mL, median intraoperative fluid volume was 2800 (419–8800) mL, and intraoperative transfusion was performed in 10 patients (9.7%). The postoperative complications were AL in 21 (20.4%) patients, organ/space SSI in 21 (20.4%), HOS in 32 (31.1%), and OO in 19 (18.4%). Grade IIIb and IV complications were found in 9 patients (8.7%), of whom 7 had AL (Table 1).

Analysis of HOS

The median onset time of HOS was postoperative day (POD) 4 (range POD 2–15), the median output volume was 2460 (1800–5450) mL, and the median maximum output volume on the onset day was 3005 (1800–5450) mL (Table 2). Organ/space SSI, AL, and OO were significant HOS-related factors in univariate analysis, and OO (odds ratio [OR] 3.82, $p = 0.022$) remained as a significantly independent factor associated with HOS in multivariate analysis (Table 3). The white blood cell (WBC) count on POD 6 was significantly higher in the HOS group than in the non-HOS group (9765 vs. 8130 /mL, $p < 0.05$) (Table 4). The WBC count on POD 3 and C-reactive protein (CRP) levels on PODs 3 and 6 were also higher in the HOS group.

Analysis of OO

The median onset time of OO was POD 4 (range POD 1–14), the median output volume was 1100 (25–3600) mL, and the median maximum output volume on the onset day was 2275 (80–4700) mL (Table 2). Organ/space SSI and HOS were significant OO-related factors in univariate analysis, but thickness of the rectus abdominis muscle did not show this relationship. Organ/space SSI (OR 3.69, $P = 0.02$) was a significantly independent factor associated with OO in multivariate analysis (Table 5). The WBC count (9400 vs. 7475 /mL, $p < 0.05$) and CRP level (6.01 vs. 2.92 mg/L, $p < 0.05$) on POD 6 were significantly higher in the OO group than in the non-OO group (Table 6). The WBC count and CRP level on POD 3 were also higher in the OO group.

Discussion

The criteria for the creation of DS vary among institutions. A meta-analysis of the significance of DS in rectal cancer showed that the anastomosis close to the anus was protected by DS [18]. A multicenter

study in Japan showed that DS did not decrease the incidence of AL, but reduced the severity [1], and three quarters of patients with AL avoided reoperation, showing the usefulness of DS. In addition, a multicenter study confirmed that oncological safety is comparable in sphincter-preserving surgery and abdominoperineal resection of locally advanced lower rectal cancer [19]. Therefore, the DS will continue to be created in patients with rectal cancer.

Intraabdominal abscess, paralytic ileus, AL and OO have previously been identified as risk factors for HOS [6–11]. Total proctocolectomy and a history of diabetes have also been suggested to be preoperative predictors of HOS [20], but these factors were not identified as significant risk factors in this study. The reported risk factors for OO are total proctocolectomy and thickness of the rectus abdominis muscle at the stoma-penetrating site [12–14]. However, these factors also had no marked relationship with OO in this study. Infection in organ/space site was associated with the causes of HOS and OO. HOS and OO were associated with the same factor which suggested similar pathology.

WBCs and CRP were examined on PODs 1, 3 and 6 as markers that reflect infectious conditions. The HOS and OO groups both had higher WBC counts and CRP levels on PODs 3 and 6 compared to the non-HOS and non-OO groups. The WBC count on POD 1 has previously been suggested to be a predictor of HOS [21], but this relationship was not significant in this study. The high WBC counts and CRP levels on PODs 3 and 6 show a prolonged postoperative infection in organ/space site, and suggest that intestinal edema and a prolonged decrease in intestinal absorption, which may be caused by infection in organ/space site, contribute to the pathology of HOS and OO. Consequently, patients with organ/space SSI due to AL should be managed with the probability of HOS and OO kept in mind. The median onset time of HOS and OO was POD 4, but some patients experienced HOS and OO on POD 1 and 2. Therefore, HOS and OO may be useful for an early sign suggesting infection in organ/space site or AL.

In terms of output volume of OO, many patients had output volume >1000 mL on the day of clinical diagnosis of OO. It may be because of prompt tube insertion in the stoma for patients with symptoms such as abdominal distension. In this study, all subjects who developed OO were fully improved by conservative treatment such as tube insertion in the oral stoma. Therefore, the OO pathology is relative stenosis of an abdominal wall-penetrating site of a stoma due to intestinal edema caused by organ/site SSI. Thus, OO should be differentiated from general structural intestinal obstruction. And it may better to say relative outlet stenosis.

The limitations of this study are its performance at a single-center study and lack of external validity. There is a possibility that OO was a real structural obstruction leading to HOS. However, the results of the study suggest that infection in organ/space site is the major cause of HOS and OO. Consequently, the most important countermeasure for reducing HOS and OO is to decrease the incidence of AL and infection in organ/space site. Intraoperative assessment of tissue perfusion during colorectal resection using ICG [22], insertion of an anal drain to decrease pressure in the anastomosed region [23], and stabilization of procedures using robotic-assisted surgery [24–26] may potentially improve outcomes. It is critical to treat organ/space infection with consideration of the possibility of HOS and OO onset.

Conclusions

HOS and OO were found in 31% and 18% of subjects who underwent colorectal surgery and DS, respectively. Infection in the organ/space was associated with the causes of HOS and OO. HOS and OO were associated with the same factor which suggested similar pathology.

Declarations

Ethics approval and consent to participate: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. The study was approved by the Ethics Committee of our institution (2018–1131).

Consent for publication: Not applicable

Availability of data and materials: The datasets used and/or analysed 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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Authors' contributions: YH and TM analyzed and interpreted the patient data. YS, HM and HN performed surgery and patient management. YH was a major contributor in writing the manuscript. KH and TM revised the manuscript. All authors given their final approval of the version to be published and agreed to be 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.

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- ## Tables
- Table 1. Clinicopathological characteristics of 103 patients

Variable	Value
Age (year)*	66 (17-82)
Gender, n (%)	
Male	82 (80)
Female	21 (20)
Body mass index (kg/m ²) *	22.9 (16.9-38.9)
Diabetes, n (%)	16 (15.5)
Smoker, n (%)	26 (25.2)
Steroid user, n (%)	6 (5.8)
Alb (g/dL)	4.2 (2.4-5)
eGFR (ml/min/1.73m ²)	74.9 (20.1-135.2)
Diameter of muscle (mm)	10.25 (5.46-19.14)
Perforation, n (%)	2 (1.9)
Stenosis, n (%)	9 (8.7)
Preoperative chemotherapy, n (%)	34 (33)
Cause of resection, n (%)	
Neoplasia	84 (81.2)
Inflammatory disease	17 (16.5)
Benign pathologies	2 (1.9)
Type of resection, n (%)	
Low anterior resection	52 (50.5)
Intersphincteric resection	31 (30.1)
Total proctocolectomy	17 (16.5)
Others	3
Approach, n (%)	
Laparoscope-assisted surgery	78 (75.7)
Robotic surgery	15 (14.6)
Open surgery	10 (9.7)
Double stapling technique, n (%)	57 (55.3)
Lateral lymph node dissection, n (%)	28 (27.2)
Operation time (min) *	319 (123-639)
Blood loss (ml) *	60 (0-3550)
Blood transfusion, n (%)	10 (9.7)
Replacement fluid volume in the operation (ml)	2800 (419-8800)
Double stapling technique, n (%)	57 (55.3)
Preoperative chemotherapy, n (%)	34 (33)
Anastomotic leakage, n (%)	21 (20.4)
Organ/space SSI, n (%)	39 (37.9)
High output stoma, n (%)	32 (31.1)
Outlet obstruction, n (%)	19 (18.4)
Complications (Clavien-Dindo), n (%)	
All (I-IV)	69 (67.0)
IIIa	12 (11.7)
IIIb	3 (2.9)
IV	6 (5.8)

* Median (range)

Table 2. Output volume about OO and HOS

	OO	HOS	non-OO↯HOS
Onset POD of HOS or OO median (range)	4 (1-14)	4 (2-15)	-
Output volume with onset day (ml) median (range)	1100 (25-3600)	2460 (1800-5450)	-
Maximum volume of stoma output (ml) median (range)	2275 (80-4700)	3005 (1800-5450)	1030 (390-3300)

HOS; high output stoma, OO; outlet obstruction, POD; post operative day

Table 3. Univariate and multivariate analyses of clinicopathological variables on High output stoma

Variables		N	Univariate analysis		Multivariate analysis	
			n (%)	P value	Odds ratio (95% CI)	P value
Age	≥65	40	15 (37.5)	0.670		
	<65	53	15 (28.3)			
Gender	Female	21	3 (14.3)	0.070		
	Male	82	29 (35.4)			
BMI (kg/m ²)	<25	25	9 (36)	0.621		
	≥25	78	23 (29.5)			
Diabetes	No	87	26 (29.9)	0.565		
	Yes	16	6 (37.5)			
Smoker	No	77	21 (27.3)	0.317		
	Yes	25	10 (40)			
Steroid user	No	97	28 (28.9)	0.073		
	Yes	6	3 (50)			
Alb	≥4.2	44	14 (31.8)	1		
	<4.2	59	18 (30.5)			
eGFR	≥60	91	30 (33.0)	0.333		
	<60	12	2 (16.7)			
Diameter of muscle (mm)	≥10.25	42	12 (28.6)	0.672		
	<10.25	61	20 (32.8)			
Neoplasia	No	19	9 (47.4)	0.105		
	Yes	84	23 (27.4)			
Perforation	No	101	31 (30.7)	0.527		
	Yes	2	1 (50)			
Stenosis	No	94	28 (29.8)	0.454		
	Yes	9	4 (44.4)			
Operation time (min)	≥319	53	20 (37.7)	0.143		
	<319	50	12 (24)			
Blood loss (ml)	≥60	50	19 (38)	0.201		
	<60	53	13 (24.5)			
Total proctocolectomy	No	86	24 (27.9)	0.153		
	Yes	17	8 (47)			
LLND	No	75	24 (32)	0.814		
	Yes	29	8 (27.6)			
Double stapling technique	No	43	17 (39.5)	0.134		
	Yes	60	15 (25)			
Preoperative chemotherapy	No	69	21 (30.4)	1		
	Yes	34	11 (32.4)			

Blood transfusion	No	93	28 (30.1)				
	Yes	10	4 (40)	0.497			
Replacement fluid volume in the operation (ml)	≥2800	53	21 (39.6)				
	<2800	50	11 (22)	0.059			
Anastomotic leakage	No	84	22 (26.2)				
	Yes	18	10 (55.6)	0.024	2.03 (7.96)	(0.52-	0.310
Organ space SSI	No	64	13 (20.3)				
	Yes	39	19 (48.7)	0.004	2.19 (6.98)	(0.69-	0.184
OO	No	84	21 (25)				
	Yes	19	11 (57.9)	0.011	3.82 (12.1)	(1.21-	0.022

BMI; body mass index, LLND; lateral lymph node dissection, SSI; surgical site infection

Table 4. 1, 3, 6 POD WBC and CRP about HOS and non-HOS

	WBC			CRP (mg/L)		
	HOS	non-HOS	p-value	HOS	non-HOS	p-value
1 POD	9670 (8200-11575)	10170 (8750-11568)	0.606	6.39 (4.35-10.30)	6.68 (4.93-8.63)	0.724
3 POD	9765 (8058-13210)	8130 (6950-100909)	0.015	13.28 (7.60-19.50)	11.787 (7.20-14.27)	0.224
6 POD	8085 (6907-9605)	7540 (6410-8725)	0.122	5.20 (1.69-10.81)	3.01 (1.70-5.71)	0.208

HOS; high output stoma, POD; post operative day, WBC; white blood cell (3300-8600), CRP; C-reactive protein (0.00-0.14)

Table 5. Univariate and multivariate analyses of clinicopathological variables on outlet obstruction

Variables		N	Univariate analysis		Multivariate analysis		
			n (%)	P value	Odds ratio (95% CI)		P value
Age	≥65	53	10 (18.9)	1	NA		
	<65	50	9 (18)				
Gender	Female	21	0 (0)	0.011			
	Male	82	19 (23.2)				
BMI (kg/m ²)	<25	25	6 (24)	0.393			
	≥25	78	13 (16.7)				
Diabetes	No	87	15 (17)	0.129			
	Yes	16	4 (25)				
Smoker	No	25	5 (20)	1			
	Yes	77	14 (18.2)				
Steroid user	No	97	18 (18.6)	0.143			
	Yes	6	1 (16.7)				
Alb	≥4.2	44	11 (25)	0.199			
	<4.2	59	8 (13.6)				
eGFR	≥60	91	15 (16.5)	0.227			
	<60	12	4 (33.3)				
Diameter of muscle (mm)	≥10.25	42	8 (19.0)	1			
	<10.25	61	11 (18)				
Neoplasia	No	19	3 (15.8)	1			
	Yes	84	16 (19.0)				
Perforation	No	101	19 (18.9)	1			
	Yes	2	0 (0)				
Stenosis	No	94	16 (17.0)	0.361			
	Yes	9	3 (33.3)				
Total proctocolectomy	No	86	16 (18.6)	1			
	Yes	17	3 (17.6)				
LLND	No	75	14 (18.37)	1			
	Yes	29	3 (10.3)				
Double stapling technique	No	43	11 (25.6)	0.129			
	Yes	60	8 (13.3)				
Preoperative chemotherapy	No	69	13 (18.8)	1			
	Yes	34	6 (17.6)				
Operation time (min)	≥319	53	10 (18.9)	1			
	<319	50	9 (18)				
Blood loss (ml)	≥60	50	10 (20)	0.801			
	<60	53	9 (17.0)				
Blood transfusion	No	93	16 (17.2)	0.388			
	Yes	10	3 (30)				
Replacement fluid volume in the operation (ml)	≥2800	53	9 (17.0)	0.801			
	<2800	50	10 (20)				
Anastomotic leakage	No	84	14 (16.7)	0.518			
	Yes	18	4 (22.2)				
Organ space SSI	No	64	6 (9.4)	0.004	3.69 (1.21-11.3)	0.022	
	Yes	39	13 (33.3)				
HOS	No	71	8 (11.3)	0.011	2.95 (0.99-8.8)	0.052	
	Yes	32	11 (34.4)				

BMI; body mass index, LLND; lateral lymph node dissection, SSI; surgical site infection

Table 6. 1, 3, 6 POD WBC and CRP about OO and non-OO

	WBC			CRP (mg/L)		
	OO	non-OO	p-value	OO	non-OO	p-value
1 POD	10950 (8835-12900)	10060 (8410-11500)	0.470	5.52 (4.20-7.91)	6.78 (4.92-9.91)	0.508
3 POD	10180 (7775-12690)	8130 (7195-10343)	0.068	14.0 (9.75-22.33)	11.73 (7.27-15.27)	0.099
6 POD	9400 (7050-10007)	7475 (6408-8810)	0.031	6.01 (2.97-11.05)	2.92 (1.50-6.49)	0.023

OO; outlet obstruction, POD; post operative day, WBC; white blood cell (3300-8600), CRP; C-reactive protein (0.00-0.14)