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# Organ/space infection is a common cause of high output stoma and outlet obstruction in diverting ileostomy

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## Abstract

**Background:** 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 significant HOS-related factors in univariate analysis, and OO (odds ratio [OR] 3.39,  $p=0.034$ ) was an independent HOS-related factor in multivariate analysis. Organ/space SSI and male were significant OO-related factors in univariate analysis, and organ/space SSI (OR 3.77,  $p=0.018$ ) was an 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.

**Keywords:** Diverting ileostomy, High output stoma, Outlet obstruction, Organ/space infection

## Background

Diverting ileostomy reduces the risk of anastomotic leakage (AL) after surgery for rectal cancer, and use of diverting ileostomy 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% [6, 7], respectively. HOS causes dehydration, electrolyte imbalance and renal dysfunction, resulting in a significant decrease of quality of

life (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 [4, 8–12]. 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,

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**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 <sup>2</sup> )*	22.9 (16.9–38.9)
Diabetes, n (%)	16 (15.5)
Smoker, n (%)	25 (24.3)
Steroid user, n (%)	6 (5.8)
Alb (g/dL)*	4.2 (2.4–5)
eGFR (ml/min/1.73m <sup>2</sup> )*	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 bowel 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 (%)	18 (17.5)
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)

but as for HOS, the pathology remains to be elucidated [13–15]. 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 diverting ileostomy 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 diverting ileostomy between December 2015 and November 2018. The study was performed as a retrospective analysis. The indications for diverting ileostomy 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 diverting ileostomy creation. The diverting ileostomy 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 ileostomy in the all patients.

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 computed tomography (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 [14]. 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

**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	50	17 (34.0)		
	< 65	53	15 (28.3)	0.670	
Gender	Female	21	3 (14.3)		
	Male	82	29 (35.4)	0.070	
BMI (kg/m <sup>2</sup> )	< 25	25	9 (36)		
	≥25	78	23 (29.5)	0.621	
Diabetes	No	87	26 (29.9)		
	Yes	16	6 (37.5)	0.565	
Smoker	No	78	22 (28.2)		
	Yes	25	10 (40)	0.323	
Steroid user	No	97	28 (28.9)		
	Yes	6	4 (66.7)	0.073	
Alb	≥4.2	44	14 (31.8)		
	< 4.2	59	18 (30.5)	1	
eGFR	≥60	91	30 (33.0)		
	< 60	12	2 (16.7)	0.333	
Diameter of muscle (mm)	≥10.25	42	12 (28.6)		
	< 10.25	61	20 (32.8)	0.672	
Neoplasia	No	19	9 (47.4)		
	Yes	84	23 (27.4)	0.105	
Perforation	No	101	31 (30.7)		
	Yes	2	1 (50)	0.527	
Stenosis	No	94	28 (29.8)		
	Yes	9	4 (44.4)	0.454	
Operation time (min)	≥319	53	20 (37.7)		
	< 319	50	12 (24)	0.143	
Blood loss (ml)	≥60	50	19 (38)		
	< 60	53	13 (24.5)	0.201	
Total proctocolectomy	No	86	24 (27.9)		
	Yes	17	8 (47)	0.153	
LLND	No	75	24 (32)		
	Yes	28	8 (28.6)	0.814	
Double stapling technique	No	43	17 (39.5)		
	Yes	60	15 (25)	0.134	
Preoperative chemotherapy	No	69	21 (30.4)		
	Yes	34	11 (32.4)	1	
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	No	85	22 (25.9)		

**Table 3** Univariate and multivariate analyses of clinicopathological variables on High output stoma (Continued)

Variables	N	Univariate analysis		Multivariate analysis		
		n (%)	P value	Odds ratio (95% CI)	P value	
leakage	Yes	18	10 (55.6)	0.023	2.25 (0.58–8.74)	0.241
Organ space SSI	No	64	13 (20.3)			
	Yes	39	19 (48.7)	0.004	1.98 (0.63–6.27)	0.245
OO	No	84	21 (25)			
	Yes	19	11 (57.9)	0.011	3.39 (1.10–10.5)	0.034

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

perforation, stenosis and preoperative chemotherapy were also examined.

Postoperative complications were analyzed using the Clavien-Dindo classification. In our institution, anastomotic infectious complications are divided into AL and organ/space surgical site infection (SSI). 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 SSI was defined clinical symptoms of intraperitoneal infection without no evidence of AL. It needs only antibiotic therapy for fever, abdominal pain and peritoneal irritation without surgical treatment.

HOS was defined as two-days continuous output of > 1500 mL per day [16]. 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 [15, 17]. 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 [18].

## 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/m<sup>2</sup>. Eighty two (80%) patients were male, 16 (15.5%) patients had diabetes, 25 (24.3%) 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 m<sup>2</sup>, 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 18 (17.5%) patients, organ/space SSI in 39 (37.9%), 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] 3.39,  $p = 0.034$ ) remained as a significantly independent factor associated with HOS in multivariate analysis (Table 3). The white blood cell (WBC) count on POD 3 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 6 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 male were significant OO-related factors in univariate analysis, but thickness of the rectus abdominis muscle did not show this relationship. Organ/space SSI (OR 3.77,  $P = 0.018$ ) 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. Out of 19 patients in the OO group, 11 patients had HOS simultaneously. In HOS and OO cases, 8 patients had organ/space SSI (72.7%).

**Discussion**

The criteria for the creation of diverting stoma vary among institutions. A meta-analysis of the significance of diverting stoma in rectal cancer showed that the anastomosis close to the anus was protected by diverting stoma [19]. A multicenter study in Japan showed that diverting stoma 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 diverting stoma. In addition, a multicenter study confirmed that oncological safety is comparable in sphincter-preserving surgery and abdominoperineal resection of locally advanced lower rectal cancer [20]. Therefore, the diverting stoma 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 [4, 8–12]. Total proctocolectomy and a history of diabetes have also been suggested to be preoperative predictors of HOS [21], 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 [13–15]. However, these factors

**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 (8200–11,575)	10,170 (8750–11,568)	0.606	6.39 (4.35–10.30)	6.68 (4.93–8.63)	0.724
3 POD	9765 (8058–13,210)	8130 (6950–100,909)	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)		
	< 65	50	9 (18)	1	
Gender	Female	21	0 (0)		
	Male	82	19 (23.2)	0.011	NA
BMI (kg/m <sup>2</sup> )	< 25	25	6 (24)		
	≥25	78	13 (16.7)	0.393	
Diabetes	No	87	15 (17)		
	Yes	16	4 (25)	0.129	
Smoker	No	25	5 (20)		
	Yes	78	14 (18.2)	1	
Steroid user	No	97	18 (18.6)		
	Yes	6	1 (16.7)	0.143	
Alb	≥4.2	44	11 (25)		
	< 4.2	59	8 (13.6)	0.199	
eGFR	≥60	91	15 (16.5)		
	< 60	12	4 (33.3)	0.227	
Diameter of muscle (mm)	≥10.25	42	8 (19.0)		
	< 10.25	61	11 (18)	1	
Neoplasia	No	19	3 (15.8)		
	Yes	84	16 (19.0)	1	
Perforation	No	101	19 (18.9)		
	Yes	2	0 (0)	1	
Stenosis	No	94	16 (17.0)		
	Yes	9	3 (33.3)	0.361	
Total proctocolectomy	No	86	16 (18.6)	1	
	Yes	17	3 (17.6)		
LLND	No	75	14 (18.67)		
	Yes	28	5 (17.9)	1	
Double stapling technique	No	43	11 (25.6)		
	Yes	60	8 (13.3)	0.129	
Preoperative chemotherapy	No	69	13 (18.8)		
	Yes	34	6 (17.6)	1	
Operation time (min)	≥319	53	10 (18.9)		
	< 319	50	9 (18)	1	
Blood loss (ml)	≥60	50	10 (20)		
	< 60	53	9 (17.0)	0.801	
Blood transfusion	No	93	16 (17.2)		
	Yes	10	3 (30)	0.388	
Replacement fluid volume in the operation (ml)	≥2800	53	9 (17.0)		
	< 2800	50	10 (20)	0.801	
Anastomotic leakage	No	85	15 (17.6)		
	Yes	18	4 (22.2)	0.518	
Organ space SSI	No	64	6 (9.4)		
	Yes	39	13 (33.3)	0.004	3.77 (1.26–11.3)

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	10,950 (8835–12,900)	10,060 (8410–11,500)	0.470	5.52 (4.20–7.91)	6.78 (4.92–9.91)	0.508
3 POD	10,180 (7775–12,690)	8130 (7195–10,343)	0.068	14.0 (9.75–22.33)	11.73 (7.27–15.27)	0.099
6 POD	9400 (7050–10,007)	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)

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 [22], 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 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.

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 infection in organ/space site. Thus, OO should be differentiated from general structural intestinal obstruction. And it may better to say relative outlet stenosis.

The limitation of this study is its performance at a single-center study and lack of external validity. There is an 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 indocyanine green (ICG) [23], insertion of an anal drain to decrease pressure in the anastomosed region [24], and stabilization of procedures using robotic-assisted surgery [25–27] may potentially improve outcomes. It is critical to treat organ/space infection with consideration of the possibility of HOS and OO onset.

## Conclusion

HOS and OO were found in 31 and 18% of subjects who underwent colorectal surgery and diverting ileostomy, 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.

## Abbreviations

AL: Anastomotic leakage; HOS: High output stoma; OO: Outlet obstruction; QOL: Quality of life; ISR: Intersphincteric resection; BMI: Body mass index; Alb: Albumin; eGFR: Estimated glomerular filtration rate; CT: Computed tomography; LLND: Lateral lymph node dissection; SSI: Surgical site infection; POD: Postoperative day; OR: Odds ratio; WBC: White blood cell; CRP: C-reactive protein; ICG: Indocyanine green

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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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## Availability of data and materials

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

## Ethics approval and consent to participate

The protocol for this research project has been approved by a suitably constituted Hirosaki University Ethics Review Committee Board and it conforms to the provisions of the Declaration of Helsinki. Approval by the Hirosaki University Ethics Review Committee Board (2018–1131) was obtained for creation and use of this de-identified database for research purposes.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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