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Predictors of High-Output Stoma After Low Anterior Resection With Diverting Ileostomy for Rectal Cancer

Jongsung Pak[1], Mamoru Uemura[1], Yasunari Fukuda[2], Masakazu Miyake[1], Masataka Ikeda[1], Kazuhiro Nishikawa[1], Atsushi Miyamoto[1], Motohiro Hirao[1], Shoji Nakamori[1], Mitsugu Sekimoto[1]

[1]*Department of Surgery, National Hospital Organization Osaka National Hospital, Osaka, Japan*

[2]*Department of Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Osaka, Japan*

Background: The aim of this study was to identify predictors of high-output stoma (HOS) after low anterior resection (LAR) with diverting ileostomy for rectal cancer.

Methods: The medical records of 60 patients who underwent LAR with diverting ileostomy for rectal cancer between 2012 and 2015 were reviewed. HOS was defined as ileostomy output greater than 1500 mL per 24 hours. Patient and surgical characteristics and patient laboratory data were examined to assess for predictors of HOS using univariate and multivariate logistic regression.

Results: The incidence of HOS was 43.3% (26/60). In univariate analysis, age $\geq$ 70 years, diabetes mellitus (DM), preoperative albumin level $\leq$ 4.0 g/dL, and preoperative serum hemoglobin level $\leq$ 12 g/dL were significantly associated with HOS. Multivariate analysis identified DM (odds ratio, 9.74; 95% confidence interval, 1.86–77.3) as an independent predictor of HOS.

Conclusions: DM might be a predictor of HOS in patients undergoing LAR with diverting ileostomy for rectal cancer.

Key words: Rectal cancer – Low anterior resection – Ileostomy – High-output stoma – Diabetes mellitus

Corresponding author: Mamoru Uemura, MD, PhD, FACS, Department of Surgery, National Hospital Organization Osaka National Hospital, 2-1-14, Houenzaka, Chuo-ku, Osaka, Osaka, 540-0006, Japan.
Tel.: +81 6 6942 1331; Fax: +81 6 6943 6467; E-mail: uemura7777@hotmail.com

Table 1 Patient characteristics

Full cohort (n = 60)	
Sex (male / female)	40 / 20
Age (years, median) [range]	65 [40–82]
BMI (kg/m^2, median) [range]	22.5 [16.9–39.5]
Smoking history (n, %)	42 (70.0)
Hypertension (n, %)	22 (36.7)
Diabetes mellitus (n, %)	11 (18.3)
Ischemic heart disease (n, %)	7 (11.7)
Preoperative chemo- and/or radiotherapy (n, %)	4 (6.7)
Preoperative decompression treatment (n, %)	0 (0)

Table 2 Preoperative blood examination

Full cohort (n = 60)	
Albumin level (median) [range]	4.2 [1.9–5.1]
Hemoglobin level (median) [range]	13.8 [9.5–16.8]
CEA level (median) [range]	4.5 [0.7–79.7]
CA19-9 level (median) [range]	11 [1–143]

Low anterior resection (LAR) is a standard surgical procedure for lower rectal cancer. Reconstruction has been facilitated by circular stapling devices.[1–3] However, postoperative complications remain an important problem. Symptomatic anastomotic leakage (AL) is the most feared complication. The incidence of LAR in patients with LAR is 1%–21%[4,5] and the mortality rate is 6%–22%.[6]

Several reports have indicated the importance of temporary diverting ileostomy to reduce anastomotic leakage–related morbidity and mortality after LAR.[7–9] However, construction of a diverting ileostomy may cause complications such as skin damage, infection, parastomal hernia, stenosis, intestinal retraction, and stoma prolapse.[10] Excessive output from the ileostomy, called high-output stoma (HOS), is also frequently observed in patients with ileostomy. HOS can lead to dehydration, renal dysfunction, and electrolyte abnormalities.[11,12] Several previous reports have indicated that patients need transfusions or medications to maintain sodium balance when stoma output reaches 1000–2000 mL/d, although there was no established definition of HOS.[13–16] To date, there have been no published reports about the risk factors for HOS.

The aim of this study was to identify predictors of HOS in patients after LAR with diverting ileostomy for rectal cancer.

Materials and Methods

A total of consecutive 112 patients underwent elective LAR with a double stapled anastomosis at Osaka National Hospital between January 1, 2012 and March 31, 2015. Among them, 65 patients underwent diverting ileostomy. Five patients were excluded because ileostomy output volume was not recorded accurately. In total, 60 patients were included in this retrospective study. HOS was defined as ileostomy output greater than 1500 mL per 24 hours in this study. The following variables were included in the analysis: patient characteristics [age, sex, body mass index (BMI), smoking history, comorbidities, history of laparotomy, and preoperative chemotherapy or chemoradiation therapy], preoperative blood examination results [serum albumin, hemoglobin, carcinogen embryonic antigen (CEA), and carbohydrate antigen 19-9 (CA19-9) levels], and surgical characteristics [laparoscopic approach or laparotomy, operative time, intraoperative blood loss volume, and epidural anesthesia]. Written informed consent was obtained from all patients for the use of their clinical data.

All statistical analyses were performed with JMP 11.0 SAS software (SAS Institute, Cary, North Carolina). All analyses were two-sided, and a P value of <0.05 was considered statistically significant. To identify factors associated with HOS, multivariate logistic regression analysis was used. Factors with a P value of <0.05 were included in the model.

The study was done in accordance with the Declaration of Helsinki (1975, as revised in 2008). The study protocol was approved by the ethics committee of National Hospital Organization Osaka National Hospital. All study participants provided written informed consent.

Results

Clinical characteristics of the study population

Table 1 shows the characteristics of the 60 patients. There were 40 males and 20 females. Median age was 66 years, and median BMI was 22.5 kg/m^2. Regarding smoking history, 42 patients (70.0%) were smokers. Their comorbidities were as follows: hypertension (HT) (n = 22, 36.7%), diabetes mellitus (DM) (n = 11, 18.3%), and history of ischemic heart disease (n = 7, 11.7%). Preoperative chemotherapy or chemoradiation therapy was performed in 4 patients (6.7%).

Table 2 shows the preoperative blood examination results of the 60 patients. Median preoperative

Table 3 Surgical procedure

Full cohort (n = 60)	
Laparoscopic surgery (n, %)	57 (95.0)
Operation time (minutes, median) [range]	358 [171–840]
Blood loss (mL, median) [range]	27.5 [0–2280]
Epidural anesthesia (n, %)	56 (93.3)
Lateral lymph node dissection (n, %)	19 (31.7)

serum albumin, hemoglobin, CEA, and CA19-9 levels were 4.2 g/dL, 13.8 g/dL, 4.5 ng/mL, and 11 U/mL, respectively.

Table 3 shows the surgical factors. Among the 60 patients, 57 (95.0%) underwent laparoscopic surgery. Median operative time and intraoperative blood loss were 358 minutes and 27.5 mL, respectively. Fifty-six patients (93.3%) received epidural anesthesia. Nineteen patients (31.7%) underwent lateral lymph node dissection for advanced lower rectal cancer according to Japanese treatment guidelines.[17]

Predictors of HOS

Among the 60 patients, HOS occurred in 26 patients (43.3%). To identify factors that are predictive of HOS, univariate analysis was performed. HOS was significantly associated with age $\geq$70 years, DM, preoperative serum albumin level $\leq$4.0 g/dL, and preoperative serum hemoglobin level $\leq$12.0 g/dL in the univariate analysis. In the multivariate analysis, which included factors with $P \leq 0.05$, DM (odds ratio, 9.74; 95% confidence interval, 1.86–77.3) was a significant independent predictor of HOS (Table 4).

Discussion

HOS is a complication frequently observed in patients with ileostomy, with a reported incidence of 16%.[11,12] Although intensive management with transfusion or medication is usually effective for maintaining homeostatic balance with HOS, it could negatively impact patients with compromised physical function, such as elderly patients. Moreover, postoperative adjuvant chemotherapy might be restricted due to uncontrollable HOS. Restriction of postoperative adjuvant chemotherapy is extremely detrimental for patients with advanced rectal cancer. Therefore, HOS should be avoided after rectal cancer surgery with diverting ileostomy. If risk factors for HOS are identified, intensive perioperative management may reduce the risk of HOS.

Previous studies have rarely analyzed which factors are predictive of HOS in patients with ileostomy. This study showed that DM is associated with HOS. Patients with preoperative albumin level $\leq$4.0 g/dL tended to have more HOS than others, although this association was not statistically significant. On the other hand, surgical characteristics were not associated with HOS.

Our data indicated that DM is an independent predictor of HOS. This may be biologically plausible because patients with DM have autonomic neuropathy of the gut.[18] They have many gastrointestinal symptoms, such as nausea, vomiting, and diarrhea. The rate of diarrhea in patients with DM has been reported as 9.5%–15.1%.[19–22] Neurogenic disorders involving the autonomic innervation of the gut is a potential mechanism of diarrhea in patients with DM.[18] The intestinal motility pattern in the fasting phase is considered to represent dysfunction of both sympathetic and parasympathetic innervation. Gastrointestinal symptoms in patients with DM were reported to be associated with poor glycemic control.[23] Therefore, preoperative management of diabetes might be important in reducing the incidence of HOS.

We identified that patients with hypoalbuminemia tended to have more HOS, although this association was not statistically significant. This may be also biologically plausible because hypoalbuminemia may cause intestinal edema and disturbance of the gastrointestinal tract. A previous study reported diarrhea occurred in 35.1% of patients with hypoalbuminemia, and hypoalbuminemia-related diarrhea was significantly more common in patients with albumin levels less than 2 g/dL.[24] For patients with hypoalbuminemia, preoperative nutritional management might useful in reducing the risk of postoperative complications including HOS.

Conclusions

We identified that DM is an independent predictor of HOS in patients undergoing LAR with ileostomy for rectal cancer.

Acknowledgments

The authors declare no conflicts of interest.

Table 4 Univariable and multivariable analysis of factors associated with HOS

Variable	n	Incidence of HOS (%)	*P* value	Odds ratio	*P*	95% CI
Age						
≥ 70	20	65.0	0.02	2.46	0.18	0.66–9.35
< 70	40	32.5	Reference			
Sex						
Male	40	50.0	0.14			
Female	20	30.0				
Smoking history						
Yes	42	51.2	0.11			
No	18	27.8				
Hypertension						
Yes	22	54.5	0.18			
No	38	36.8				
Diabetes mellitus						
Yes	11	81.8	< 0.01	9.74	< 0.01	1.86–77.30
No	49	34.7	Reference			
Ischemic heart disease						
Yes	7	71.4	0.11			
No	53	40.4				
Laparotomy history						
Yes	19	31.6	0.21			
No	41	48.8				
Preoperative therapy						
Yes	4	75.0	0.18			
No	56	41.1				
Pre-op albumin level						
≤ 4.0	20	65.0	0.02	3.59	0.07	0.91–14.87
> 4.0	40	32.5	Reference			
Pre-op hemoglobin level						
≤ 12.0	12	75.0	0.01	2.75	0.23	0.54–16.30
> 12.0	48	35.4	Reference			
Surgical approach						
Laparoscopy	57	43.9	0.72			
Laparotomy	3	33.3				
Operation time (min)						
≥ 350	31	51.6	0.18			
< 350	29	34.5				
Blood loss (mL)						
≥ 30	30	50.0	0.30			
< 30	30	36.7				

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