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Association Between Advanced T Stage and Thick Rectus Abdominis Muscle and Outlet Obstruction and High-Output Stoma After Ileostomy in Patients With Rectal Cancer

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Objective: This study aimed to identify factors associated with outlet obstruction and high-output stoma (HOS) after ileostomy creation.

Summary of background data: Ileostomy creation is effective in preventing leakage among patients undergoing low anterior resection for rectal cancer. However, major complications such as outlet obstruction and HOS can occur after surgery. Moreover, these complications cannot be prevented.

Methods: This retrospective study included 34 patients with rectal cancer who underwent low anterior resection and ileostomy creation at Okayama University Hospital from January 2015 to December 2018. Then, the risk factors associated with outlet obstruction and HOS were analyzed.

Results: Of 34 patients, 7 (21%) experienced outlet obstruction. In a multivariate logistic regression analysis, advanced T stage ($P = 0.10$), ileostomy with a short horizontal diameter ($P = 0.01$), and thick rectus abdominis (RA) muscle ($P = 0.0005$) were considered independent risk factors for outlet obstruction. There was a significant correlation between outlet obstruction and HOS ($P = 0.03$). Meanwhile, the independent risk factors of HOS were advanced T stage ($P = 0.03$) and thick RA muscle ($P = 0.04$).

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Conclusions: Thick RA muscle and advanced T stage were the common risk factors of outlet obstruction and HOS. Therefore, in high-risk patients, these complications can be prevented by choosing an appropriate ileostomy location according to RA muscle thickness and by preventing tubing into the ileostomy.

Key words: Muscle – Ileostomy – Complications – Risk factors

Colorectal cancer (CRC), one of the most common malignancies worldwide, is the second leading cause of cancer-related deaths in western countries.[1] The National Comprehensive Cancer Network guidelines recommend surgical treatment for patients with CRC without distant metastasis.[2] However, the complication rate of rectal cancer surgery is higher than that of colon cancer surgery.[3] Anastomotic leakage is one of the most severe surgical complications. When low anterior resection is performed for rectal cancer, an ileostomy is often created to prevent anastomotic leakage.[4,5] Temporal ileostomy is often established at the right side of the abdomen, via the right rectus abdominis (RA) muscle, to prevent parastomal hernia.[6] Then, the ileostomy is closed several months after rectal resection.

Ileostomy creation is effective in preventing leakage. However, surgeons must pay attention to the complications of ileostomy itself. Outlet obstruction, which can result in ileus, and high-output stoma (HOS), which can lead to dehydration, are the 2 major complications of ileostomy. However, they cannot be prevented.

Hence, the current study aimed to identify factors associated with outlet obstruction and HOS after ileostomy. We believe that the findings of this research can help prevent such complications.

Materials and Methods

Patients

This retrospective study included 34 patients with rectal cancer who underwent low anterior resection of the rectum and ileostomy creation at Okayama University Hospital from 2015 to 2018. The diagnosis of CRC was confirmed based on clinicopathologic findings. The tumor, node, metastasis staging system of the American Joint Committee on Cancer was used for pathologic tumor staging. Patients with distant metastasis were excluded from the analysis. This study was approved by the institutional review board of Okayama University (Approval 1905-002). All methods were performed in accordance with the relevant guidelines and regulations.

Creation of ileostomy

The skin flap with a diameter of 2 cm was initially cut, and subcutaneous fat was cut up to the fascia of the RA muscle sheath. An incision on the muscle was made, and the RA muscle was split wide enough to accommodate 3 fingers into the abdominal cavity. Finally, the terminal ileum was pulled up to the skin level, and a loop ileostomy was created.

Measurement of RA muscle thickness

The RA muscle was located at the anterior part of the abdomen. RA muscle thickness was measured via computed tomography (CT) scan. Preoperative CT scan images were obtained from all patients. Those who presented with outlet obstruction or HOS after surgery underwent repeat CT scan. RA muscle thickness at the internal side of the ileostomy was retrospectively measured via CT scan before and after the occurrence of outlet obstruction (Fig. 1). Even if there were no complications, CT scan images were obtained during surveillance, which was performed within 3 months after surgery.

Statistical analysis

Data were expressed as mean ± standard deviation (SD). Between-group differences were assessed using the Wilcoxon's rank-sum test or the χ^2 test, as appropriate. Receiver operating characteristic (ROC) curves were constructed to determine the cutoff values for analyzing the risk factors of outlet obstruction using the Youden index. Univariate and multivariate logistic regression analyses were performed. The JMP software (version 10.0, SAS Institute Inc, Cary, North Carolina) was used in all analyses. All P values were 2-sided. $P \leq 0.1$ indicated a risk, and $P \leq 0.05$ was considered statistically significant.

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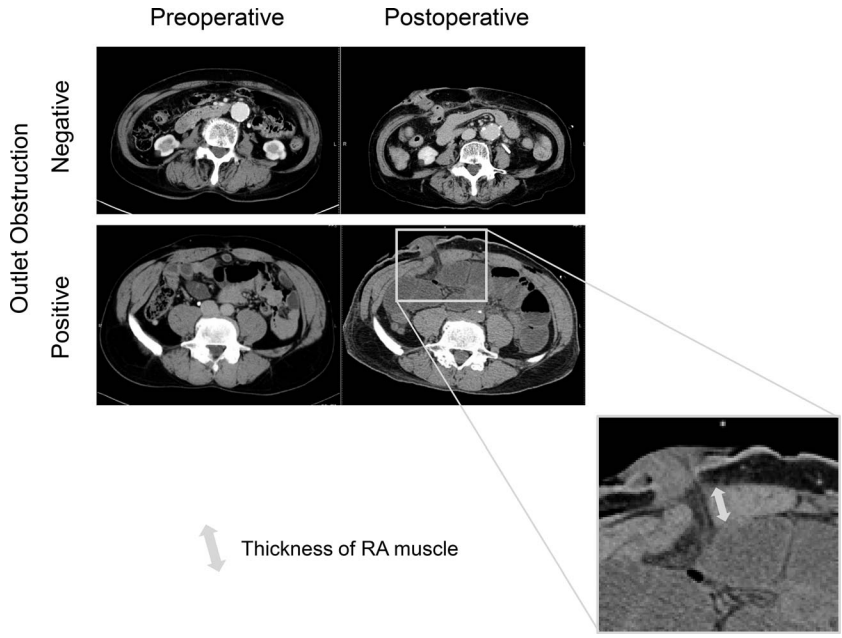

Fig. 1 Clinical parameters correlated with outlet obstruction after ileostomy. The RA muscle thickness was retrospectively measured at the internal side of the ileostomy via CT scan.

Results

Advanced T stage and anatomic feature of ileostomy as risk factors of outlet obstruction after ileostomy creation

This retrospective study included 34 patients with rectal cancer who underwent low anterior resection of the rectum and ileostomy creation. Of 34 patients, 7 (21%) experienced outlet obstruction (Table 1).

Outlet obstruction was associated with male sex ($P = 0.04$), advanced T stage ($P = 0.05$), postoperative high white blood cell count ($P = 0.005$), high preoperative neutrophil count ($P = 0.04$), ileostomy with a short horizontal diameter ($P = 0.0004$), and thick RA muscle ($P < 0.0001$).

The univariate logistic regression analysis showed that male sex ($P = 0.01$), advanced T stage ($P = 0.04$), high postoperative white blood cell count ($P = 0.01$), high preoperative neutrophil count ($P = 0.07$), ileostomy with a short horizontal diameter ($P = 0.001$), and thick RA muscle ($P < 0.0001$) were risk factors for outlet obstruction. Then, the multivariate logistic regression analysis revealed that advanced T stage ($P = 0.10$), ileostomy with a short horizontal diameter ($P = 0.01$), and thick RA muscle ($P = 0.0005$) were independent risk factors for outlet obstruction (Table 2). Hence, advanced T stage and anatomic feature of the ileostomy might be risk factors for outlet obstruction after ileostomy.

Outlet obstruction after ileostomy as a risk factor of HOS

Outlet obstruction and HOS are important complications of ileostomy. Thus, the relationship between outlet obstruction and HOS was examined. HOS was defined as an ileostomy discharge volume of >1500 mL. This condition was assessed at postoperative days 3, 4, and 5 in the outlet obstruction positive and negative groups.

The ileostomy discharge volume was higher in the outlet obstruction positive group than in the outlet obstruction negative group (day 3, $P = 0.06$; day 4, $P = 0.03$; day 5, $P = 0.007$; Fig. 2A). The risk of HOS in patients with an ileostomy discharge volume of >1500 mL was higher in the outlet obstruction positive group than in the outlet obstruction negative group (day 3, $P = 0.05$; day 4, $P = 0.02$; day 5, $P = 0.06$; Fig. 2B). Therefore, outlet obstruction might be a risk factor of HOS.

Advanced T stage and anatomic feature of ileostomy as risk factors of HOS

Whether advanced T stage and anatomic feature of ileostomy are also associated with HOS, which was significantly correlated with outlet obstruction, was examined.

HOS was correlated with a high body mass index (BMI; $P = 0.07$), advanced T stage ($P = 0.02$), high preoperative white blood cell count ($P = 0.06$), high postoperative white blood cell count ($P = 0.07$), high

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Table 1 Association between clinicopathologic characteristics and outlet obstruction

Variables	*n*	Outlet obstruction: Negative ($n = 27$)	Outlet obstruction: Positive ($n = 7$)	*P*
Physical parameter				
Sex				
Male	23	16	7	0.04[a]
Female	11	11	0	
Age (years)				
<70[b]	21	15	6	0.14
≥70	13	12	1	
BMI (kg/m^2)				
<25.7[c]	29	22	7	0.21
≥25.7	5	5	0	
Tumor				
Location				
Ra	8	5	3	0.18
Rb	26	22	4	
Pathologic T category				
pT1/2	16	15	1	0.05[a]
pT3/4	18	12	6	
Lymph node metastasis				
Absent	27	22	5	0.56
Present	7	5	2	
Treatment				
Neoadjuvant chemo				
Absent	21	15	6	0.14
Present	13	12	1	
Laparoscopic or open				
Open	2	2	0	0.46
Laparoscopic	32	25	7	
Operative time (min)				
<388[c]	30	24	6	0.82
≥388	4	3	1	
Anastomotic complication				
Absent	30	25	5	0.12
Present	4	2	2	
Blood examination				
Preoperative WBC count (/μL)				
<5050[c]	13	12	1	0.13
≥5050	20	14	6	
Postoperative WBC count (/μL)				
<11,600[c]	29	25	4	0.005[a]
≥11,600	4	1	3	
Preoperative neutrophil count (%)				
<72.5[c]	30	25	5	0.04[a]
≥72.5	3	1	2	
Postoperative neutrophil count (%)				
<82.6[c]	25	21	4	0.13
≥82.6	7	4	3	
Preoperative CRP count (mg/dL)				
<0.79[c]	31	24	7	0.45
≥0.79	2	2	0	
Postoperative CRP count (mg/dL)				
<13.5[c]	22	19	3	0.13
≥13.5	11	7	4	
Ileostomy				
Horizontal diameter (mm)				
<10.8[c]	5	1	4	0.0004[a]
≥10.8	29	26	3	
Craniocaudal diameter (mm)				
<35[c]	31	25	6	0.57
≥35	3	2	1	
Postoperative RA muscle thickness (mm)				
<14.5[c]	26	25	1	<0.0001[a]
≥14.5	8	2	6	

CRP, C reactive protein; WBC, white blood cell.

[a]$P \leq 0.05$.

[b]The median age at surgery was 70 years in this cohort.

[c]The cutoff value was calculated using the Youden index.

postoperative neutrophil count ($P = 0.08$), and thick RA muscle ($P = 0.02$; Table 3).

The univariate logistic regression analysis showed that a high BMI ($P = 0.07$), advanced T stage ($P = 0.02$), high preoperative white blood cell count ($P = 0.05$), high postoperative white blood cell count ($P = 0.07$), high postoperative neutrophil rate ($P = 0.08$), ileostomy with a long craniocaudal diameter ($P = 0.10$), and thick RA muscle ($P = 0.02$) were risk factors for HOS. Then, the multivariate logistic regression analysis revealed that advanced T stage ($P = 0.03$) and thick RA muscle ($P = 0.04$) were independent risk factors for HOS (Table 4). Thus, advanced T stage and anatomic feature of ileostomy might also be risk factors for HOS, similar to outlet obstruction.

Treatment of outlet obstruction and HOS

Patients with outlet obstruction or HOS were treated with tubing into the ileostomy. Both outlet obstruction and HOS did not extend duration to stoma closure (Supplementary Fig. 1), suggesting that both phenomena are short-term complications.

Role of ileostomy location in preventing outlet obstruction and HOS after ileostomy creation

Advanced T stage and thick RA muscle were found to be the common risk factors of outlet obstruction and HOS. Although the relationship between these 2 phenomena is challenging to confirm, the outlet obstruction–HOS cycle theory might play a role (Fig. 3A).

This phenomenon can be caused by incomplete ileostomy obstruction mainly because of a thick RA muscle causing high resistance. Because of incomplete obstruction, the volume of upper intestinal secretion

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Table 2 Univariate and multivariate analyses of the predictors of outlet obstruction

	Univariate analysis		Multivariate analysis	
Variables	OR	*P*	OR	*P*
Physical parameter				
Sex (male)	1.61e+8	0.01[a]	4.10	1.00
Age (<70 years[b])	4.80	0.12		
BMI (<25.7 kg/m^2)[c]	4.0.3e+7	0.11		
Tumor				
Location (Ra)	3.30	0.20		
Pathologic T category (pT3/4)	7.50	0.04[a]	1.69e+14	0.10
Lymph node metastasis (present)	1.76	0.57		
Treatment				
Neoadjuvant chemotherapy (absent)	4.80	0.12		
Laparoscopic or open (laparoscopic)	3.05e+6	0.33		
Operative time (≥388 min)[c]	1.33	0.82		
Anastomotic complication (present)	5.00	0.16		
Blood examination				
Preoperative WBC count (≥5050/μL)[c]	5.14	0.11		
Postoperative WBC count (≥11,600/μL)[c]	18.75	0.01[a]	2.31	1.00
Preoperative neutrophil count (≥72.5%)[c]	10.00	0.07		
Postoperative neutrophil count (≥82.6%)[c]	3.94	0.15		
Preoperative CRP count (≥0.79 mg/dL)[c]	3.15e−7	0.32		
Postoperative CRP count (≥13.5 mg/dL)[c]	3.62	0.14		
Ileostomy				
Horizontal diameter (<10.8 mm)[c]	34.7	0.001[a]	5.84e+14	0.01[a]
Craniocaudal diameter (≥35 mm)[c]	2.08	0.59		
Postoperative RA muscle thickness (≥14.5 mm)[c]	75.0	<0.0001[a]	1.59e+15	0.0005[a]

CRP, C reactive protein; OR, odds ratio; WBC, white blood cell.

[a]$P \leq 0.05$.

[b]The median age at surgery was 70 years in this cohort.

[c]The cutoff value was calculated using the Youden index.

increases, thereby resulting to mucosal edema. Although the volume of ileostomy discharge is enough, the condition of the intestinal fluid reservoir worsens because of fluid supply overload. Then, progressive relative ileostomy obstruction occurs. In addition, advanced T stage induces preoperative intestinal obstruction, edema, and inflammation, leading to HOS and relative outlet obstruction. This hypothesis is supported by elevated white blood cell count ($P = 0.05$) in patients with advanced CRC (Table 5). After the initiation of the outlet obstruction–HOS cycle, it will be difficult to inhibit the development of outlet obstruction and HOS, and ileostomy drainage via tubing will be required.

Because thick RA muscle can cause outlet obstruction, we believe that the most important factor is ileostomy location. Based on a cross-sectional assessment, the RA muscle has a flat, oval shape, and it is thinner at the lateral side. Thus, even if a patient has a thick RA muscle, when an ileostomy is created at the lateral side, the thickness of the RA muscle adjacent to the ileostomy will be lower than that at the middle, thereby preventing outlet obstruction and HOS after ileostomy (Fig. 3B). Considering that pipe flow resistance is proportional to its length and inversely proportional to its diameter (Darcy–Weisbach equation), our hypothesis can be supported by the theory of fluid mechanics.[7]

Discussion

The current study found a significant correlation between outlet obstruction and HOS and low anterior resection in patients with rectal cancer who had an ileostomy. Furthermore, the common risk factor of outlet obstruction and HOS is a thick RA muscle. Patients with a thick RA muscle had a high incidence rate of outlet obstruction and HOS. Thus, RA muscle thickness is a predictive marker of outlet obstruction and HOS. In addition, advanced T stage causes preoperative intestinal obstruction, edema, and inflammation, leading to HOS and relative outlet obstruction. High-risk patients with advanced CRC and thick RA muscle will require a clinical counterplan to prevent these complications.

Recent advancements in the treatment of rectal cancer are remarkable, and developments in laparoscopic surgery have been outstanding within the last decade.[8–11] However, anastomotic procedures have not significantly changed. The double-stapling technique using linear and circular staplers is the most common approach.[12] The risk of leakage is dependent on anastomosis location, and the risk

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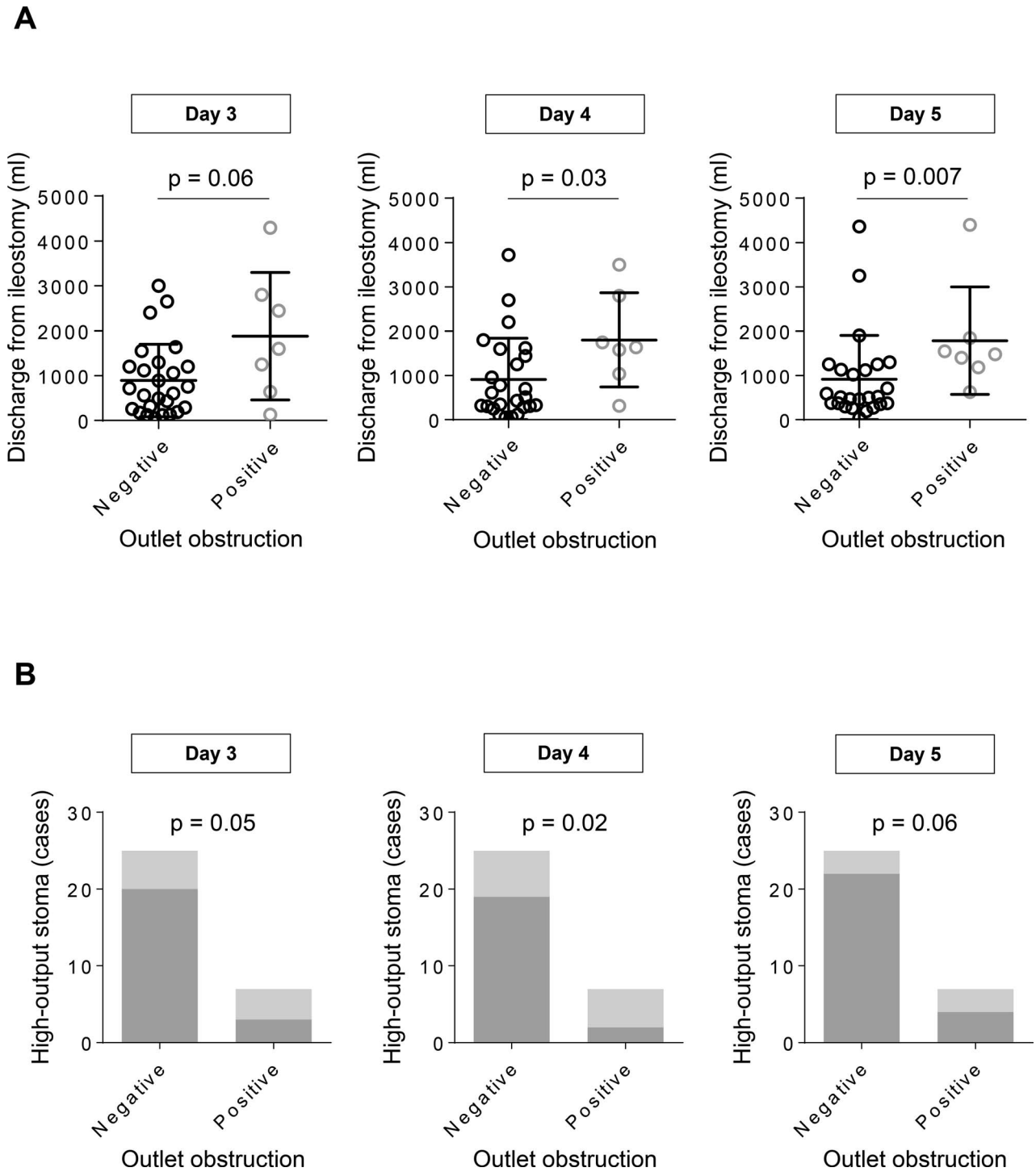

Fig. 2 Relationship between outlet obstruction and high-output stoma after ileostomy. (A) The volume of ileostomy discharge was higher in the outlet obstruction positive group than in the outlet obstruction negative group (Wilcoxon's signed-rank test). (B) The risk of high-output stoma among patients with an ileostomy discharge volume of >1500 mL was higher in the outlet obstruction positive group than in the outlet obstruction negative group (χ^2 test).

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Table 3 Association between clinicopathologic characteristics and high-output stoma

Variables	*n*	High-output stoma (day 4) Negative ($n = 21$)	Positive ($n = 11$)	*P*
Physical parameter				
Sex				
Male	21	12	9	0.16
Female	11	9	2	
Age (years)				
<70[b]	20	12	8	0.39
≥70	12	9	3	
BMI (kg/m^2)				
<25.7[c]	28	20	8	0.07
≥25.7	4	1	3	
Tumor				
Location				
Ra	8	5	3	0.83
Rb	24	16	8	
Pathologic T category				
pT1/2	15	13	2	0.02[a]
pT3/4	17	8	9	
Lymph node metastasis				
Absent	25	17	8	0.59
Present	7	4	3	
Treatment				
Neoadjuvant chemotherapy				
Absent	20	13	7	0.92
Present	12	8	4	
Laparoscopic or open				
Open	2	2	0	0.29
Laparoscopic	30	19	11	
Operative time (min)				
<388[c]	29	19	10	0.97
≥388	3	2	1	
Anastomotic complication				
Absent	29	20	9	0.22
Present	3	1	2	
Blood examination				
Preoperative WBC count (/μL)				
<5050[c]	13	11	2	0.06
≥5050	19	10	9	
Postoperative WBC count (/μL)				
<11,600[c]	28	20	8	0.07
≥11,600	4	1	3	
Preoperative neutrophil count (%)				
<72.5[c]	29	20	9	0.22
≥72.5	3	1	2	
Postoperative neutrophil count (%)				
<82.6[c]	25	18	7	0.08
≥82.6	6	2	4	
Preoperative CRP level (mg/dL)				
<0.79[c]	30	20	10	0.63
≥0.79	2	1	1	
Postoperative CRP level (mg/dL)				
<13.5[c]	22	16	6	0.21
≥13.5	10	5	5	
Ileostomy				
Horizontal diameter (mm)				
<10.8[c]	5	3	2	0.77
≥10.8	27	18	9	
Craniocaudal diameter (mm)				
<35[c]	29	18	11	0.19
≥35	3	3	0	
Postoperative RA muscle thickness (mm)				
<14.5[c]	25	19	6	0.02[a]
≥14.5	7	2	5	

CRP, C reactive protein; WBC, white blood cell.

[a]$P \leq 0.05$.

[b]The median age at surgery was 70 years in this cohort.

[c]The cutoff value was calculated using the Youden index.

increases when the anastomotic site is adjacent to the dentate line. An ileostomy is usually created to prevent anastomotic leakage.[4,5] Even if the anastomosis between the residual rectum and sigmoid colon is incomplete, an ileostomy can stabilize the anastomotic site.[13]

Although ileostomy creation is effective in preventing anastomosis, the prevention of outlet obstruction and HOS is extremely challenging. Moreover, information about these complications is limited, and their causes and solutions remain unknown.[14–18] The incidence rates of outlet obstruction and HOS were 7.7% to 8.7% and 23% to 45%, respectively.[18–22] The risk factors of outlet obstruction are type of surgery, old age, thick subcutaneous fat, and high white blood cell count.[21] In addition, abdominal sepsis, short bowel, obstruction, drugs, overload with intravenous saline solution, enteritis, diabetes mellitus, proctocolectomy, and high white blood cell count have been associated with HOS.[18,19,23–25] However, there is no consistent theory that can explain the cause of outlet obstruction and HOS and the association between them.

The current study showed that both outlet obstruction and HOS were associated with a thick RA muscle, causing high resistance for passage and advanced T stage, resulting in intestinal obstruction and edema. Thick RA muscle and advanced T stage were independent risk factors of both outlet obstruction and HOS. Considering this clinical evidence, we proposed the outlet obstruction–HOS cycle theory, which links thick RA muscle and

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Table 4 Univariate and multivariate analyses of the predictors of high-output stoma

Variables	Univariate analysis		Multivariate analysis	
	OR	*P*	OR	*P*
Physical parameter				
Sex (male)	3.38	0.15		
Age (<70 years[b])	2.00	0.38		
BMI (≥25.7kg/m^2)[c]	7.5	0.07		
Tumor				
Location (Ra)	1.2	0.83		
Pathologic T category (pT3/4)	7.31	0.02[a]	6.88	0.03[a]
Lymph node metastasis (present)	1.59	0.60		
Treatment				
Neoadjuvant chemotherapy (absent)	1.08	0.92		
Laparoscopic or open (laparoscopic)	5.98e+7	0.33		
Operative time (<388 min)[c]	1.05	0.97		
Anastomotic complication (present)	4.44	0.23		
Blood examination				
Preoperative WBC count (≥5050/μL)[c]	4.95	0.05		
Postoperative WBC count (≥11,600/μL)[c]	7.50	0.07		
Preoperative neutrophil count (≥72.5%)[c]	4.44	0.23		
Postoperative neutrophil count (≥82.6 %)[c]	5.14	0.08		
Preoperative CRP level (≥0.79 mg/dL)[c]	2.00	0.64		
Postoperative CRP level (≥13.5 mg/dL)[c]	2.67	0.21		
Ileostomy				
Horizontal diameter (<10.8 mm)[c]	1.33	0.78		
Craniocaudal diameter (<35 mm)[c]	7.53e+7	0.10		
Postoperative RA muscle thickness (≥14.5 mm)[c]	7.92	0.02[a]	7.35	0.04[a]

CRP, C reactive protein; OR, odds ratio; WBC, white blood cell.

[a]$P \leq 0.05$.

[b]The median age at surgery was 70 years in this cohort.

[c]The cutoff value was calculated using the Youden index.

Table 5 Association between clinicopathologic characteristics and pathologic T stage

Variable	*n*	Pathologic T category		*P*
		pT1/2 (*n* = 16)	pT3/4 (*n* = 18)	
Treatment				
Laparoscopic or open				
Open	2	0	2	0.17
Laparoscopic	32	16	16	
Operative time (min)				
<388[b]	30	14	16	0.90
≥388	4	2	2	
Anastomotic complication				
Absent	30	14	16	0.90
Present	4	2	2	
Blood examination				
Preoperative WBC count (/μL)				
<5050[b]	13	9	4	0.05[a]
≥5050	20	7	13	
Postoperative WBC count (/μL)				
<11,600[b]	29	15	14	0.32
≥11,600	4	1	3	
Preoperative neutrophil count (%)				
<72.5[b]	30	16	14	0.08
≥72.5	3	0	3	
Postoperative neutrophil count (%)				
<82.6[b]	25	13	12	0.27
≥82.6	7	2	5	
Preoperative CRP level (mg/dL)				
<0.79[b]	31	16	15	0.16
≥0.79	2	0	2	
Postoperative CRP level (mg/dL)				
<13.5[b]	22	12	10	0.32
≥13.5	11	4	7	
Ileostomy				
Horizontal diameter (mm)				
<10.8[b]	5	2	3	0.73
≥10.8	29	14	15	
Craniocaudal diameter (mm)				
<35[b]	31	14	17	0.48
≥35	3	2	1	
Preoperative RA muscle thickness (mm)				
<11.2[b]	23	14	9	0.007[a]
≥11.2	10	1	9	
Postoperative RA muscle thickness (mm)				
<14.5[b]	26	14	12	0.15
≥14.5	8	2	6	

CRP, C reactive protein; WBC, white blood cell.

[a]$P \leq 0.05$.

[b]The cutoff value was calculated using the Youden index.

advanced T stage and outlet obstruction and HOS. To prevent this cycle among high-risk patients with a thick RA muscle and advanced CRC, the ileostomy should be created at the thinner lateral side of the RA muscle to reduce resistance for discharge flow. In addition, preventive tubing to avoid ileostomy obstruction may be effective in inhibiting the progression of the outlet obstruction–HOS cycle.

The current study had a limitation. That is, only retrospective analyses were performed. Currently, we are planning to perform a prospective study, in which an ileostomy will be created at the thinner lateral side of the RA muscle in patients with a thick RA muscle. Then, the incidence rates of obstruction

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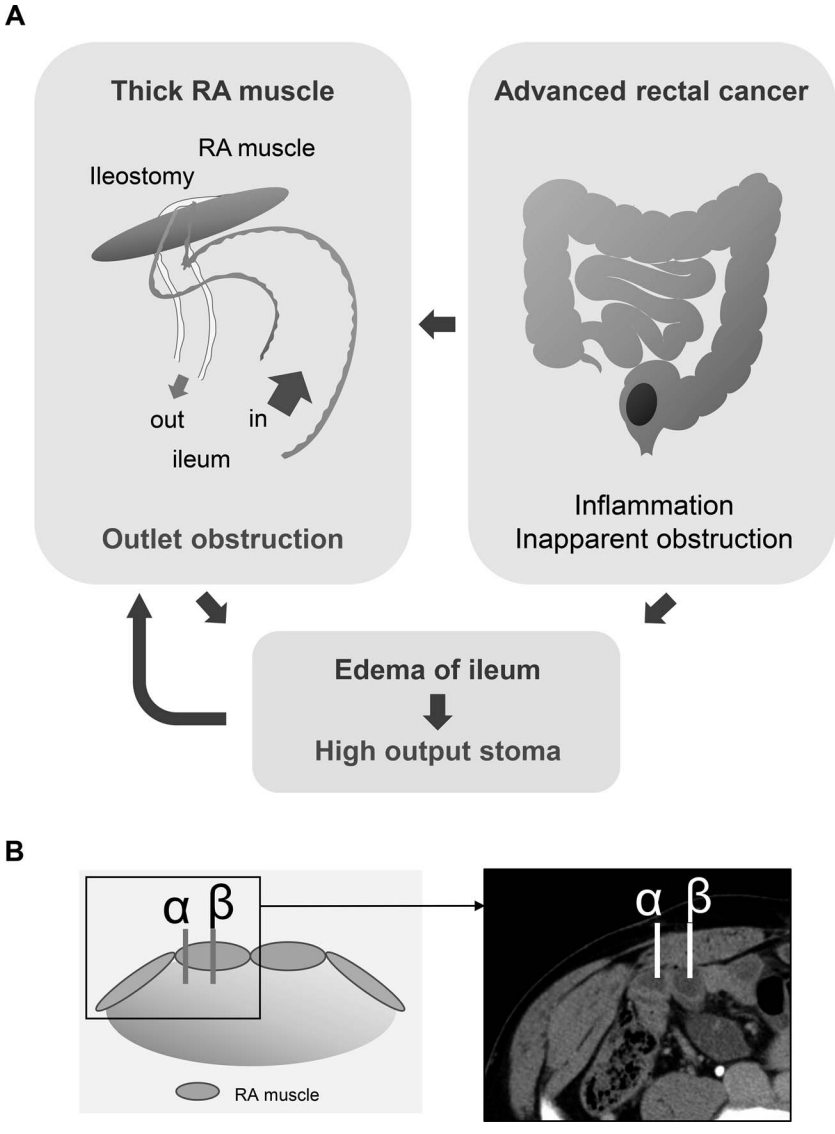

Fig. 3 Association between thick RA muscle and outlet obstruction and high-output stoma. (A) The outlet obstruction–HOS cycle theory. (B) When an ileostomy was created at the lateral side (α), the thickness of RA muscle adjacent to the ileostomy was lower than that at the middle (β), thereby preventing outlet obstruction and HOS after ileostomy.

and HOS will be compared between control and experiment groups.

Conclusions

Thick RA muscle and advanced T stage were associated with outlet obstruction and HOS after ileostomy. In high-risk patients, these complications can be prevented by choosing an appropriate ileostomy location according to RA muscle thickness and by preventing tubing into the ileostomy.

Acknowledgments

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