

Incidence and risk factors for rectal pain after laparoscopic rectal cancer surgery

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Abstract

Objective: This study was performed to investigate the incidence of and potential risk factors for rectal pain after laparoscopic rectal cancer surgery.

Methods: We retrospectively analyzed data from 300 patients who underwent laparoscopic rectal cancer surgery. We assessed the presence of rectal pain and categorized patients into Group N (no rectal pain) or Group P (rectal pain).

Results: In total, 288 patients were included. Of these patients, 39 (13.5%) reported rectal pain and 14 (4.9%) had rectal pain that persisted for >3 months. Univariate analysis revealed that patients in Group P had more preoperative chemoradiotherapy, more ileostomies, longer operation times, more anastomotic margins of <2 cm from the anal verge, more anastomotic leakage, and longer hospital stays. Multivariate analysis identified an anastomotic margin of <2 cm from the anal verge and a long operation time as risk factors. The presence of diabetes mellitus was a negative predictor of rectal pain.

Conclusions: In this study, the incidence of rectal pain after laparoscopic rectal cancer surgery was 13.5%. An anastomotic margin of <2 cm from the anal verge and a long operation time were risk factors for rectal pain. The presence of diabetes mellitus was a negative predictor of rectal pain.

Thus, the possibility of postoperative rectal pain should be discussed preoperatively with patients with these risk factors.

Keywords

Anastomosis, laparoscopic surgery, rectal cancer, rectal pain

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Introduction

Despite rapid advancement in surgical techniques, laparoscopic rectal cancer surgery is still associated with a higher rate of complications than other laparoscopic colectomies.¹ The increased rate of complications is likely due to the difficult anatomic position of this surgery; the pelvis is narrow, resulting in a high risk of damage to the autonomic and/or somatic pelvic nerve plexus.¹⁻⁴ Common postoperative complications include anastomotic leakage, urinary and sexual dysfunction, perirectal abscess, prolonged ileus, rectovaginal fistula, and wound infection or dehiscence.^{2,5} Acute postoperative pain is also an expected outcome. In patients who have undergone abdominal surgery, the pain manifests as a deep visceral pain inside the abdomen and/or parietal pain in the abdominal wall.⁶ The estimated risk of chronic postsurgical pain is about 17% for laparoscopic colorectal surgery, depending on the indication for the surgery.^{6,7} Intraoperative nerve damage and/or perioperative chemoradiotherapy (CRT) may also contribute to persistent postoperative pain.^{8,9} However, some patients experience rectal pain for unclear reasons. Such pain can negatively affect the patients' overall life quality and may be extremely costly.³ Follmar et al.¹⁰ suggested that a neural origin should be considered in the differential diagnosis of rectal pain if the onset of pain is related to previous surgery of the anus or rectum. The aim of this study was to determine the incidence of and risk factors for rectal pain after laparoscopic rectal cancer surgery.

Patients & Methods

Patients

This study was approved by our departmental ethics committee (2014-12-067) and

registered with the Clinical Research Information Service (<http://cris.cdc.go.kr>, ref: KCT0001359). We retrospectively reviewed the electronic medical records of 300 patients who underwent elective laparoscopic rectal surgery from 2013 to 2014 in a single center. The patients ranged in age from 25 to 87 years. All patients had tumors located within 15 cm of the anal verge and underwent laparoscopic low anterior resection or anterior resection. The exclusion criteria were emergency surgery, a history of abdominal surgery, recurrent rectal lesions, metastatic rectal lesions, conversion to open laparotomy, and a lack of follow-up data.

Interventions

All surgeries were performed by one of six specialized colorectal surgeons who followed similar techniques, and tumor-specific mesorectal excision according to the tumor location was adopted as the standard surgical technique for rectal cancer. A double-stapling technique was applied for transanal anastomosis. Ileostomy for protection of low rectal anastomosis was performed at the surgeon's discretion. All patients underwent general anesthesia and postoperative pain control with a patient-controlled analgesia device. The patient-controlled analgesia regimen involved fentanyl (1500 µg) and normal saline in a total volume of 100 ml. If postoperative analgesia was felt to be inadequate at any time, intravenous fentanyl, hydromorphone, or pethidine was supplied. Opioid consumption was recorded by conversion to fentanyl units throughout the operation and then again at 1 h, 1 day, 3 days, and 5 days postoperatively. Patient demographics, preoperative CRT, type of surgical resection, operation time, pathological stage, maximum tumor size, anastomotic margin from the anal verge, performance of

ileostomy, postoperative complications, and length of hospital stay were analyzed. Postoperative abdominal pain was defined as pain that was located inside the abdomen and/or abdominal wall. Postoperative rectal pain was defined as pain that was located around the perineum with/without radiation to the lower extremities and that was not a continuation of preoperative pain. The pain included either somatic nociceptive or neuropathic characteristics (burning, shooting, or lancinating pain) or both. In the postoperative period, independent nurses evaluated abdominal and rectal pain using a numeric rating scale (0 = no pain, 10 = worst pain imaginable) at 1 h, 1 day, 3 days, 5 days, 1 month, 3 months, 6 months, and 12 months postoperatively. Chronic pain was defined as pain that persisted for at least 3 months postoperatively after exclusion of other causes of pain such as wound infection and/or malignancy.

Statistical analysis

All data were analyzed using SAS 9.4 (SAS Institute, Cary, NC, USA). Data are expressed as mean \pm SD or frequency and proportion, as appropriate. Intergroup differences were assessed using Fisher's exact test and the Mann-Whitney U test. Variables measured at different time points were compared using repeated-measures analysis of variance, with Bonferroni post hoc correction performed when appropriate. The potential risk factors for postoperative rectal pain were examined by univariate and multivariate analyses. A *P* value of <0.05 was considered to indicate statistical significance.

Results

In total, 300 patients were enrolled in this study; however, 12 met the exclusion criteria (2 patients were diagnosed with distant metastasis, 5 underwent open laparotomy, and 5 were lost to follow-up). Thus,

288 patients were included in the final analysis. Rectal pain was evaluated from the first 1 h postoperatively (Table 1). The demographic data and surgical characteristics are summarized in Table 2. Patients who experienced rectal pain at least once during the study period comprised Group P ($n = 39$). Patients without rectal pain comprised Group N ($n = 249$) (Table 2).

Univariate analysis

Age, sex, height, weight, body mass index, Charlson comorbidity index, pathological stage, and mean tumor size did not differ significantly between the two groups. Preoperative CRT was more frequently performed in Group P than Group N ($P < 0.001$). Moreover, Group P had longer operation times ($P < 0.001$), more ileostomies ($P = 0.001$), more anastomotic margins of < 2 cm from the anal verge ($P < 0.001$), longer hospital stays ($P = 0.013$), and more anastomotic leakage ($P = 0.013$) than did Group N (Table 2).

Multivariate analysis

Factors with a *P* value of < 0.1 in the univariate analysis, including the presence of diabetes mellitus, performance of

Table 1. Rectal pain onset ($n = 39$).

Postoperative time point	
1 h	5 (12.8)
1 d	3 (7.7)
3 d	11 (28.2)
5 d	8 (20.5)
1 mo	6 (15.4)
3 mo	3 (7.7)
6 mo	3 (7.7)
12 mo	0 (0.0)

All data are presented as *n* (%) patients.

Table 2. Potential predictive factors for rectal pain.

	All patients (n = 288)	Group N (n = 249)	Group P (n = 39)	Univariate		Multivariate		
				95% CI	P value	95% CI	P value	OR
Age, years	60.7 ± 11.1	61.0 ± 11.1	58.3 ± 11.0	0.949–1.008	0.148			
< 60	125 (43.4)	104 (41.8)	21 (53.9)					
≥ 60	163 (56.6)	145 (58.2)	18 (46.2)					
Sex, M/F	177/111	153/96	24/15	0.502–2.009	0.991			
Height, cm	162.1 ± 8.6	161.9 ± 8.5	163.5 ± 9.6	0.982–1.065	0.478			
Weight, kg	60.7 ± 10.5	60.5 ± 10.5	61.7 ± 10.5	0.979–1.044	0.497			
BMI, kg/m ²	23.0 ± 3.0	23.0 ± 3.0	23.0 ± 3.2	0.903–1.128	0.877			
< 25	218 (75.7)	187 (75.1)	31 (79.5)		0.553			
≥ 25	70 (24.3)	62 (24.9)	8 (20.5)					
Charlson comorbidity index	2.9 ± 1.5	2.9 ± 1.5	3.0 ± 1.6	0.863–1.324	0.545			
Presence of diabetes mellitus	46 (16.0)	44 (17.7)	2 (5.1)		0.064	1.107–28.980	0.037	5.663
Preoperative CRT	63 (21.9)	46 (18.5)	17 (43.6)*	1.678–6.931	<0.001	0.431–3.111	0.771	1.158
Pathological stage								
I	104 (36.1)	88 (35.3)	16 (41.0)	0.123–9.781	0.450			
II	54 (18.8)	48 (19.4)	6 (15.4)	0.077–7.338				
III	104 (36.1)	93 (37.5)	11 (28.2)	0.078–6.452				
IV	25 (8.7)	19 (7.7)	6 (15.4)	0.189–19.039				
Preoperative pain (NRS)	0.6 ± 1.8	0.2 ± 1.1	0.3 ± 1.2	1.008–1.018	0.830			
Operation time, min	177.0 ± 61.3	168.6 ± 55.1	230.4 ± 72.1*	1.489–6.229	<0.001	1.006–1.018	<0.001	1.012
Ileostomy	61 (24.5)	45 (18.6)	16 (41.0)*	0.384–1.708	0.001			
Maximum tumor size of > 4 cm	92 (36.9)	81 (32.7)	11 (28.2)	3.155–14.683	0.580			
Anastomotic margin of ≤ 2 cm from anal verge	39 (15.7)	23 (9.2)	16 (41.0)*		<0.001	2.475–13.542	<0.001	5.790
Length of hospital stay, days	7.7 ± 5.4	7.4 ± 4.3	10.1 ± 9.7*	1.013–1.117	0.013	0.966–1.109	0.324	1.035
Anastomotic leakage	13 (4.5)	8 (3.2)	5 (12.8)*	1.370–14.326	0.013	0.454–12.280	0.306	2.362

All data are presented as mean ± SD or n (%). patients. M/F: male/female; BMI: body mass index; CRT: chemoradiotherapy; NRS: numeric rating scale; CI: confidence interval; OR: odds ratio; Group N: patients without postoperative rectal pain; Group P: patients with postoperative rectal pain. *p < 0.05 compared with Group N.

Table 3. Abdominal pain severity and opioid consumption.

	Group N (n = 249)	Group P (n = 39)	P value
Pain severity (NRS)			
1 h postoperatively	5.5 ± 1.0	5.6 ± 1.1	0.794
1 d postoperatively	5.9 ± 1.5	6.1 ± 2.2	0.484
3 d postoperatively	4.5 ± 1.8	5.1 ± 2.0	0.084
5 d postoperatively	3.3 ± 1.2	3.9 ± 2.0	0.125
Opioid consumption, µg			
Intraoperative	87.0 ± 52.0	90.2 ± 55.9	0.737
1 h postoperatively	49.9 ± 26.6	52.6 ± 31.4	0.627
1 d postoperatively	80.8 ± 77.1	109.2 ± 130.8	0.194
3 d postoperatively	80.5 ± 82.8	115.5 ± 133.5	0.120
5 d postoperatively	79.0 ± 49.3	118.6 ± 79.0*	0.004

All data are presented as mean ± SD. Group N: patients without postoperative rectal pain; Group P: patients with postoperative rectal pain; NRS: numeric rating scale. * $P < 0.05$ compared with Group N.

preoperative CRT, a long operation time, an anastomotic margin of <2 cm from the anal verge, and anastomotic leakage, were entered into a multivariate model. Multivariate stepwise logistic regression analysis revealed that an anastomosis margin of <2 cm from the anal verge ($P < 0.001$, OR = 5.790, CI = 2.475–13.542) and a long operation time ($P < 0.001$, OR = 1.012, CI = 1.006–1.018) were significantly associated with rectal pain (Table 2). The presence of diabetes mellitus ($P = 0.037$, OR = 5.663, CI = 1.007–28.980) was a negative predictor of rectal pain (Table 2). Among these findings, an anastomotic margin of <2 cm from the anal verge showed the highest odds ratio for predicting rectal pain.

Incidence and management of postoperative pain

Of all 288 patients, 33 (13.5%) reported rectal pain that developed within 1 month after surgery. Six patients (2.1%) reported rectal pain that developed 3 months after surgery (Table 1). The overall opioid consumption was significantly higher in Group

P than Group N on postoperative day 5 (Table 3). Fourteen patients (4.9%) had chronic rectal pain that persists more than 3 months (Table 4). These patients had undergone multiple treatments including anticonvulsants, antidepressants, opioids, and/or rehabilitation exercise (Table 4).

Discussion

Surgical incisions result in tissue damage, subsequent inflammation, and postoperative pain. Although most patients heal without long-term sequelae, several types of surgery such as amputation, thoracotomy, and mastectomy involve obligatory neurologic injury, often leading to a cascade of postinjury sensitization and chronic pain.¹¹ Rectal tumor resection is a painful surgery. Postsurgical rectal pain may be due to somatic pain from the surgical incision, visceral pain from the intra-abdominal structures, and neuropathic pain from the pelvic plexus.¹² Gilliland et al.¹³ found that surgical procedures, including colectomy, were the most frequently cited precipitating factors (19.8%) for the development of

Table 4. Continued.

Patient No.	Postoperative time point											
	1 h	1 d	3 d	5 d	1 mo	3 mo	6 mo	12 mo				
13	0	0	0	0	Opioids	0	Observation	0	3	Opioids	3	Observation
14	0	PCA	0	0	Opioids	0		2	Observation	0	0	Observation
15	0	PCA	0	0	Opioids	5		0	Observation	0	0	Observation
16	0	PCA	4	0	Opioids			0	Observation			
17	0	PCA	0	2	Opioids	4	Opioids	4	Observation	2	Rehabilitation	Observation
18	0	PCA	6	0	Opioids	0		0	Observation	0	2	Observation
19	0	PCA	6	0	Opioids			0	Observation			
20	3	PCA	0	0	Opioids	0		0	Observation	3	Rehabilitation	Observation
21	0	PCA	0	6	Opioids			0	Observation			
22	0	PCA	4	0	Opioids			0	Observation			
23	0	PCA	0	0	Opioids	5		5	Observation	5	2	Rehabilitation
24	0	PCA	3	0	Opioids			0	Observation	Opioids		
25	0	PCA	0	0	Opioids	4		5	Observation	5	3	
26	0	PCA	4	0	Opioids	4		1	Opioids	4	3	Rehabilitation

(continued)

Table 4. Continued.

Patient No.	Postoperative time point											
	1 h	1 d	3 d	5 d	1 mo	3 mo	6 mo	12 mo				
27	0	0	0	0		4		0	Observation	0	0	0
28	0	0	0	Opioids					Observation			
				4					0			
29	0	0	0	Opioids					Observation			
				5					0			
30	0	0	0	Opioids					Observation			
				4					0			
31	0	0	6	Opioids					Observation			
				0					0			
32	0	0	6	Opioids					Observation			
				0					0			
33	0	4	0	Opioids					Observation			
				4					0			
35	0	0	0	Opioids					Observation			
				0				5			6	
36	0	0	0	Opioids					Observation			
				0				0			3	
37	7	0	0	Opioids					Observation			
				0							0	
38	0	0	0	Opioids								
				3							0	
39	5	0	0	Opioids								
				0							0	
				Opioids					Observation			

Pain severity is presented as the numeric rating scale score. PCA: patient-controlled analgesia.

intractable rectal pain. Similarly, Atkin et al.¹⁴ found that anal surgery was the most common initiating event and often led to chronic pain and a hypersensitive rectum. However, the pathophysiological mechanisms of postoperative rectal pain have not yet been analyzed. Neural damage during surgery is a well-recognized risk factor for chronic neuropathic pain.⁶ In particular, neuropathic cancer pain can be present following cancer-directed therapy.¹⁵ Central processing of pain signals from peripheral acute trauma or inflammation is a proposed factor.¹⁶ Moreover, surgery-induced peripheral neuromodulation in the pelvic cavity and anal canal can influence the spinal cord and cerebral cortex.

In the present study, the incidence of rectal pain after laparoscopic rectal cancer surgery was 13.5%. Bouman et al.¹⁷ reported that severe acute postsurgical pain is a predictor of chronic postsurgical pain. Although the perioperative pain scores were not significantly different between the two groups in the present study, Group P consumed a significantly greater amount of opioids. This may be expected because the goal of rescue analgesics is to avoid pain escalation. We also found that an anastomotic margin of <2 cm from the anal verge and a long operation time were positive predictors of postoperative rectal pain. Sensory fibers to the anus are usually present in the anal canal, particularly in the region of the anal valves.¹⁸ Thus, damage to this area may result in much greater pain than damage to other areas because of the increased nociceptive sensitivity in the anal canal. Additionally, prolonged traction and electrocoagulation during surgery can damage the neural plexus of the abdominopelvic cavity. Neuropathic pain induced by intraoperative nerve injury has been proposed as a major cause of chronic postoperative pain.¹⁹ A long operation time can increase the possibility of intraoperative nerve injury, which affects acute and chronic

postoperative pain. Visceral afferent and somatic fibers from the distal rectum, anus, and perineum may project to the ganglion impar, which is the most caudal ganglion of the sympathetic trunk. These neuron bundles have been implicated in sympathetically mediated pain in the pelvis, which is characterized by poorly localized pain with a burning quality and sense of urgency.²⁰ Anorectal postsurgical physiological alterations may also be related to this phenomenon. Disruption of neuromuscular continuity within the rectal wall leads to rectal sensation and compliance abnormalities and can also interfere with the intramural rectoanal reflex.^{4,21} This disruption can also cause functional changes such as impaired absorption and impaired secretory function, resulting in rectal discomfort and/or pain. The anal sphincter integrity, rectoanal sensation, rectal compliance, neuronal innervation, stool consistency, and bowel mobility can also be altered after surgery, affecting rectal pain.²²

The presence of diabetes mellitus was a negative predictor of rectal pain in the present study. Although the mechanisms of sensory changes in patients with diabetes mellitus are not fully known, we suspect that loss of intraepidermal nerve fibers and disturbance of peripheral nerve regeneration are associated with altered rectal pain perception.²³

We also considered preoperative CRT, the intraoperative inflammatory response, and postoperative anastomotic leakage as potential inflammatory factors.²⁴⁻²⁷ In the present study, Group P underwent more preoperative CRT and experienced more postoperative leakage, although the differences in these factors between the two groups were not significant in our multivariate analysis. Exposure of normal tissue to radiation can generate a sustained and uncontrolled inflammatory response.^{24,25} Although many afferent fiber bundles innervating internal organs appear to contain unresponsive afferent fibers, these fibers

become activated in the presence of injury, ischemia, and/or inflammation.^{12,26} In combination with preoperative primed inflammation, these intraoperative and postoperative inflammatory cascades potentiate nerve sensitivity, leading to postoperative neuropathic pain.^{25–27}

This study has several limitations. First, we did not assess preoperative anal sphincter function; perioperative bowel symptoms such as frequency, urgency, incontinence, diarrhea, and constipation; the postoperative condition of the anal skin; or postoperative colonoscopy findings. Another limitation is that we did not assess psychosocial factors such as preoperative expectations regarding postoperative pain, pain anxiety, and anxiety sensitivity, all of which can influence postoperative pain. Additionally, this study was retrospective in nature and was therefore potentially biased. Despite these limitations, this is the first attempt to quantify the incidence of rectal pain and identify its related risk factors following laparoscopic rectal cancer surgery. Because a low distal anastomotic margin and long operation time were found to be positive predictors in our study, we recommend preoperative discussions and active perioperative analgesic strategies as preemptive and preventive treatments. Our findings also warrant future well-controlled, prospective randomized trials for reducing pain.

In conclusion, rectal pain after laparoscopic rectal cancer surgery was significantly associated with a low anastomotic margin from the anal verge and a long operation time. Our findings suggest that increased attention should be given to the development of rectal pain and that sufficient pain management strategies are needed to effectively prevent postsurgical rectal pain.

Supplementary materials

Jin Young Lee: study design, data collection and analysis, writing and revision of the

manuscript. Hee Cheol Kim, Jung Wook Huh: providing criticism of the manuscript. Woo Seog Sim: study design, data collection and analysis, writing and revision of the manuscript. Hyun Young Lim, Eun Kyung Lee, Hui Gyeong Park, Yu Jeong Bang: data collection.

Declaration of conflicting interest

The authors declared that there is no conflict of interest.

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