외과학 석사 학위논문

Resting vector volume measured before ileostomy reversal may be a predictor of major fecal incontinence in patients with mid or low rectal cancer: A longitudinal cohort study using a prospective clinical database

중하부직장암 환자의 회장루 복원 전 항문내압검사의 휴식기 벡터 부피를 이용한 변실금 환자의 예측에 관한 연구

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서울대학교 대학원
의학과 외과학 전공
김 민 현

Abstract

Resting vector volume measured before ileostomy reversal may be a predictor of major fecal incontinence in patients with mid or low rectal cancer: A longitudinal cohort study using a prospective clinical database

Kim Min Hyun
Department of Surgery
The Graduate School
Seoul National University

Background: Despite a high incidence of fecal incontinence following sphincter-preservation surgery (SPS), there are no definitive factors measured before ileostomy reversal that predict fecal incontinence. We investigated whether vector volume anorectal manometry before ileostomy reversal predicts major fecal incontinence following SPS in patients with mid or low rectal cancer.

Methods: This longitudinal prospective cohort study comprised 173 patients who underwent vector volume anorectal manometry before ileostomy reversal. The Fecal Incontinence Severity Index was measured one year after primary SPS and classified as major incontinence (FISI score ≥25) or continent/minor incontinence (FISI score <25). Multivariable logistic regression analysis was used to identify predictors of major incontinence.

Results: Ninety-two patients (53.1%) had major incontinence. Although tumor stage, location, and neoadjuvant chemoradiotherapy were comparable, the major incontinence group had lower resting pressure (28.4 vs. 34.3 mmHg, P = 0.027), greater asymmetry at rest (39.1% vs. 34.1%, P = 0.002) and squeezing (34.2% vs. 31.4%, P = 0.046), shorter sphincter length (3.3 vs. 3.7 cm, P = 0.034), and lower resting vector volume (143,601 vs. 278,922 $mmHg^2$•mm, P < 0.001) compared with the continent/minor incontinence group. Resting vector volume was the only independent predictor of major incontinence (odds ratio = 0.675 per 100,000 $mmHg^2$•mm, 95% confidence interval, 0.532–0.823; P = 0.006).

Conclusions: This study revealed that resting vector volume before ileostomy reversal may predict major fecal incontinence. We suggest that the physiology of the anorectum should be discussed with patients before ileostomy reversal in patients at high risk of fecal incontinence.

Key words: Anorectal manometry, Ileostomy reversal, Fecal incontinence

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Introduction

Sphincter-preservation surgery is now widely performed since the introduction of total mesorectal excision [1], the development of circular surgical staplers [2], and the application of pre-operative chemoradiotherapy [3], which do not compromise the patient's oncologic outcomes. However, fecal incontinence is common after sphincter-preservation surgery for mid or low rectal cancer [4] and is a major issue owing to its significant negative impact on the patient's quality of life [5, 6]. The development of fecal incontinence may be related to radiotherapy, proximity of the tumor to the anal verge, advanced stage, and history of a diverting ostomy [7-9], because these factors may alter the morphology and physiology of the anorectum and sphincter complex.

Anorectal manometry may be a useful tool to objectively assess the function of the anal canal. However, none of the manometric parameters are definitive predictors of major fecal incontinence before ileostomy reversal. Although some patients with fecal incontinence after rectal surgery show changes in manometry pressure, rectal capacity, or rectal compliance or asymmetry of the anal sphincter [10-15], these findings are not consistent among studies. Vector volume manometry, a measurement utilizing the three-dimensional profilometric pressure measurements across the anal sphincter, may be more advantageous than conventional manometry due to its assessment of the vector component across the anal sphincter [16, 17]. The purpose of this study was to investigate the diagnostic value of vector volume manometry for predicting major fecal incontinence before ileostomy reversal in patients with mid or low rectal cancer.

Materials and Methods

Patients

This was a longitudinal study of a prospective database comprising of patients who underwent ileostomy reversal at Seoul National University Bundang Hospital between March 2005 and May 2016. The cohort included patients who initially underwent sphincter-preservation surgery for mid (5–10 cm from the anal verge) or low (0–5 cm from the anal verge) rectal cancer, and who underwent vector volume anorectal manometry before ileostomy reversal. Ileostomy formation is routinely performed at our institution for mid or low rectal cancer patients with colorectal anastomosis within 5cm from the anal verge. Patients with anastomosis higher than this are assessed for risk of anastomotic leak and ileostomy is formed for high risk patients. Ileostomy reversal was scheduled for patients with no evidence of the disease after complete surgical recovery and/or termination of adjuvant chemotherapy. Patients were evaluated for anastomosis integrity and ileostomy reversal was not performed if there were any signs of leak or threatening signs. Patients with locally advanced rectal cancer underwent neoadjuvant chemoradiotherapy in accordance with National Comprehensive Cancer Network guidelines [18]. Neoadjuvant therapy was normally performed for patients with magnetic resonance image (MRI) findings with either of the following; T3 lesions stage with involvement of circumferential resection margin (CRM) regardless of N, T4 lesions regardless of N stage, or other signs of locally advanced rectal cancer such as presence of extramural venous invasion or lateral pelvic lymph node. Sphincter-preservation surgery was done either laparoscopically or using an open method. The decision to undergo sphincter-preservation surgery was made by the clinician with the patient's consent. Patients who underwent abdominoperineal resection for lesions invading the anal sphincter were excluded from the cohort. Anastomosis was made using an endoluminal stapler or by hand-sewn methods. During the stapling procedure, the surgeon took care to avoid wedging any sphincter muscles or pelvic floor muscles during approximation of the anvil, resulting in near-circular anastomosis.

All patients completed the translated version (Fig. 1) of the Fecal Incontinence Severity Index (FISI) questionnaire via individual interviews at 1 year after rectal cancer resection [19]. Patients were divided into two groups according to their FISI score: major incontinence (FISI score ≥25) or continent/minor incontinence (FISI score <25) [5, 20-25]. Although there is no consensus on the exact definition of major fecal incontinence based on the FISI score, we used FISI score ≥25 to define major incontinence partly based on a previous study where patients with FISI score ≥25 showed a significant decrease in their quality of life [5] and partly based on the median FISI score in our cohort. We compared the manometric parameters recorded before ileostomy reversal between the two groups. General demographic and surgical data were compared between the two groups, including the following: age, sex, body mass index (BMI), tumor location, tumor stage, radiotherapy, chemotherapy, sphincter-preservation surgery approach, operation type, and anastomotic technique. Patients with fecal incontinence were treated with various medications and dietary/exercise education methods; however, did not undergo any means of invasive treatments such as nerve stimulation. This study was approved by the Institutional Review Board of our institution (Protocol no. B-1808-484-105)

Fecal Incontinence Severity Index(FISI)
최근 한 달 동안의 상황에 대해 귀하와 가장 가깝다고 생각하시는 한 가지만 표기(V)해 주십시오.

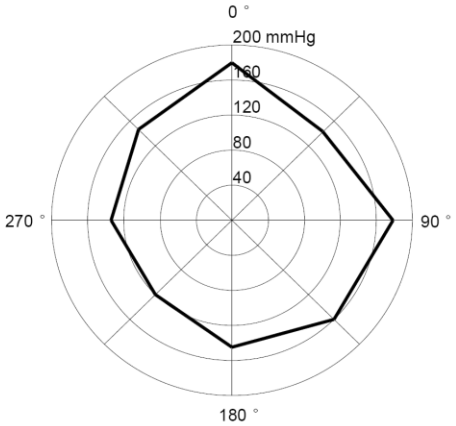
	하루에 2회 이상	하루에 한 번	일주일에 2번 이상	일주일에 한 번	한 달에 1-3번	한 달에 한번미만	전혀 없다
가스							
코같은 점액							
설사변							
고형변							

Fig. 1 Translated version of the Fecal Incontinence Severity Index questionnaire used in the study.

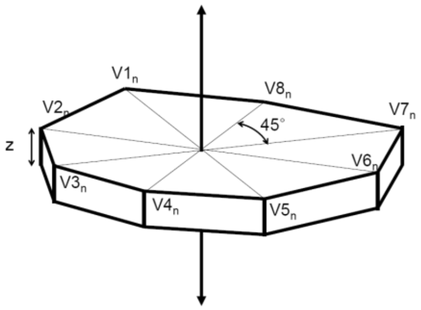
Anorectal Manometry

Anorectal manometry was conducted in an outpatient clinic before the patient was admitted for ileostomy reversal, as in our prior study [14]. All manometry measurements were performed with a water-perfusion technique using an eight-channel Micro Tip catheter (Medtronic, Minneapolis, MN) connected to a perfusion pump. Patients were held in the left-lateral position with their hips flexed at 90°. The probe was positioned 6 cm from the anal verge and pressure was measured using a continuous pull-through method at 0.25 cm/s. The following anorectal parameters were recorded: mean resting pressure, percentage asymmetry at rest, maximal squeezing pressure, percentage asymmetry at squeezing, sustained duration, sphincter length, high pressure zone (HPZ) length, defecation index, coughing reflex, and vector volume at rest. Anorectal sensation tests of compliance were not performed after restorative proctectomy because of the risk of bowel perforation [26]. Vector volume parameters were defined as previously described [27]. The percentage asymmetry of the sphincter was defined as the percentage of the deviation of the integrated cross-sections from a perfect circle. The HPZ length was defined as the length of the sphincter at which pressures of ≥50% above the basal pressure were recorded during a sustained squeeze. The resting vector volume is the vector volume of the anal canal measured at rest, which is calculated by adding up the segmental vector volumes across the anal canal (Fig. 1 & 2). Each segmental vector volume is the product of the radial area multiplied by each segmental z-axis length. The radial area is the area of the measurements made by the profilometric profile of a given segment. Typically, for an eight-channel probe, it would be the sum of the multiplied product of each adjacent probe and then multiplied by 0.354 [27]. The resulting vector volume was calculated by the Polygram software (Medtronic GI, Minneapolis, MN) and was given in $mmHg^2mm$.

a

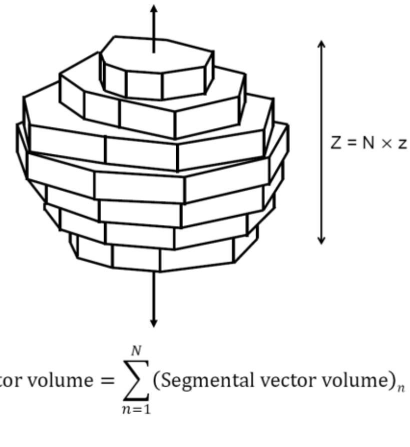


b



$$(\text{Segmental vector volume})_n = \frac{z}{2\sqrt{2}}(V1_n \times V2_n + V2_n \times V3_n + \cdots . V8_n \times V1_n)$$

c



$$\text{Vector volume} = \sum_{n=1}^{N} (\text{Segmental vector volume})_n$$

Fig. 1 Diagram of vector volume measurement. a: example of an 8-probe pressure vector reading of a given segment *n*. b: segmental vector volume of the *n* segment is the product of the radial area multiplied by the segmental z-axis length. c: vector volume is the sum of all the segmental vector volumes across the z-axis (*i.e.* the anal canal).

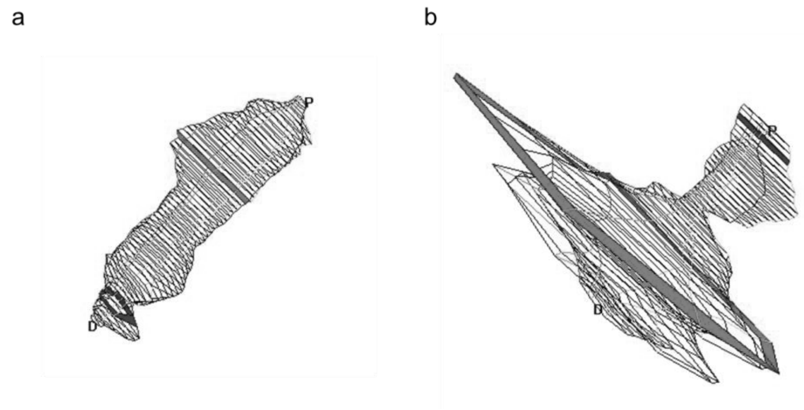


Fig. 2 Resting vector volume in a representative patient with major incontinence (a; FISI score ≥25) and in a continent patient (b; FISI score = 0). The red ring represents the segment with the maximal segmental vector volume and the blue ring represents the segment with the minimal segmental vector volume of a given measurement. P, proximal portion of the anal canal; D, distal end of the anal canal

Statistical Analysis

Quantitative variables are expressed as the mean ± standard deviation for normally distributed variables or as the median (interquartile range [IQR]) for non-normally distributed variables. The $\chi 2$ test and Student's t-test (Mann–Whitney U test for non-normally distributed variables) were used to compare categorical and continuous variables, respectively, between the two groups. Anorectal manometry parameters were compared using Student's t-test between the major and minor incontinence groups. Univariable and multivariable logistic regression analyses were also used to assess which manometric parameters were predictors of major incontinence. Parameters with $P < 0.25$ in univariable analyses were included in the multivariable analysis, in which $P < 0.05$ was considered statistically significant. A predictive cutoff value of resting vector volume was then calculated using receiver-operating characteristic (ROC) curve analyses by calculating the area under the ROC curve (AUC). The optimal thresholds were determined by maximizing the Youden index. Statistical analyses were performed using SPSS version 20.0 (Chicago, IL) and MedCalc 15.6.1 (Mariakerke, Belgium).

Results

Patient Characteristics

A total of 173 patients with available manometry measurements before ileostomy reversal and 1-year post-operative FISI score were included in the study cohort. Their median age was 60.0 years (range 33–82 years) and 112 (64.7%) were male. Tumor location was low in 134 (77.5%) patients and pre-operative chemoradiotherapy was performed in 115 (71.6%) patients. Laparoscopic surgery was performed in 117 (67.6%) patients. Stapled anastomosis and hand-sewn anastomosis were done in 111 (64.2%) and 62 (35.8%) cases, respectively. Ileostomy repair was performed at a median of 5.6 months (IQR 4.7–6.4 months) after primary resection.

On the basis of the FISI score, there were 92 patients in the major incontinence group and 81 patients in the continent/minor incontinence group; the median FISI score was 26 (IQR 12.5–32.0) in the overall cohort, 31 (IQR 29–37) in the major incontinence group, and 12 (IQR 0–20) in the continent/minor incontinence group. Baseline clinical and tumor characteristics including sex, BMI, tumor location, and stage were comparable in both groups (Table 1). However, the mean age was greater in the major incontinence group (62.1 ± 10.2 vs. 57.2 ± 11.4 years). The proportions of patients who underwent preoperative radiotherapy or chemotherapy were similar in both groups. The operation type, surgical approach, and anastomosis type were also similar in both groups. The proportion of each component of the FISI score to each corresponding group is shown in Table 2.

Table 1 Baseline characteristics

	Major incontinence (n = 92)	Continent/minor incontinence (n = 81)	P
Age, years, median (range)	62 (37–80)	59 (33–82)	0.005
Sex, n (%)			0.437
Male	62 (67.4)	50 (61.7)	
Female	30 (32.6)	31 (38.3)	
BMI[a]	23.3 ± 3.0	24.1 ± 3.1	0.096
Tumor location, cm from the anal verge, median (IQR[b])	4.0 (3.0–5.9)	5.0 (3.0–5.0)	0.556
Low rectum (0–5 cm), n (%)	68 (73.9)	66 (81.5)	0.276
Mid rectum (5.1–10cm), n (%)	24 (26.1)	15 (18.5)	
Pathologic tumor stage, n (%)			0.777
0	10 (10.9)	14 (17.3)	
1	35 (38.0)	30 (37.0)	
2	13 (14.1)	12 (14.8)	
3	30 (32.6)	22 (27.2)	
4	4 (4.3)	3 (3.7)	

Distal resection margin, cm	1.8 ± 1.5	1.7 ± 1.4	0.818
Radiotherapy, *n* (%)			0.324
None	30 (32.6)	21 (25.9)	
Preoperative	57 (62.0)	58 (71.6)	
Postoperative	5 (5.4)	2 (2.5)	
Chemotherapy, *n* (%)			0.347
None	16 (17.4)	16 (19.8)	
Postoperative	19 (20.7)	9 (11.1)	
Surgical approach, *n* (%)			0.105
Open	35 (38.0)	21 (25.9)	
Laparoscopic	57 (62.0)	60 (74.1)	
Operation type, *n* (%)			0.088
Low anterior resection	16 (17.4)	6 (7.4)	
Ultra-low anterior resection	49 (53.3)	54 (66.7)	
Intersphincteric resection	27 (29.3)	21 (25.9)	
Anastomosis, *n* (%)			0.346
Hand-sewn	36 (39.1)	26 (32.1)	
Stapled	56 (60.9)	55 (67.9)	

[a]BMI, body mass index; [b]IQR, interquartile range

Table 2 Frequency according to types of incontinence in continent/minor incontinence group and major incontinence group

Type of incontinence		Frequency of incontinence during the past one month, *n* (%)					
		≥2/day	1/day	≥2/week	1/week	1–3 /month	Less frequent/never
Major incontinence (*n* = 92)	Gas	63 (68.5)	6 (6.5)	10 (10.9)	1 (1.1)	2 (2.2)	10 (10.9)
	Mucous	9 (9.8)	3 (3.3)	2 (2.2)	3 (3.3)	10 (10.9)	65 (70.7)
	Liquid	15 (16.3)	7 (7.6)	17 (18.5)	7 (7.6)	9 (9.8)	37 (40.2)
	Solid	43 (46.7)	12 (13.0)	16 (17.4)	5 (5.4)	5 (5.4)	11 (12.0)
Continent/ minor incontinence (*n* = 81)	Gas	14 (17.3)	3 (3.7)	13 (16.0)	0	11 (13.6)	40 (49.4)
	Mucous	0	0	2 (2.5)	0	7 (8.6)	72 (88.9)
	Liquid	1 (1.2)	0	5 (6.2)	5 (6.2)	13 (16.0)	57 (70.4)
	Solid	2 (2.5)	2 (2.5)	9 (11.1)	2 (2.5)	13 (16.0)	53 (65.4)

Anorectal Manometry Analysis

Anorectal manometry was performed before ileostomy reversal at a median of 4.8 months (IQR 3.9–5.8 months) after primary rectal resection. Patients who underwent sphincter-preservation surgery had lower resting and squeezing pressures, higher asymmetry at rest and squeezing, and lower mean resting vector volume compared with previously reported values in a historical healthy control group that were assessed using the same protocol and equipment at our institution (mean resting pressure: 56.4 ± 14.2 mmHg; resting asymmetry: 29.8 ± 8.2%; maximum squeezing pressure: 141.7 ± 53.8 mmHg, squeeze asymmetry: 28.4 ± 9.9%; high pressure zone length: 2.1 ± 0.8 cm; mean resting vector volume: 460,709 ± 410,368 mmHg2•mm) [14]. In our cohort, we found that resting pressure, resting vector volume, and sphincter length were lower in the major incontinence group than in the continent/minor incontinence group. Asymmetry at rest and asymmetry at squeezing were greater in the major incontinence group. However, maximal squeezing pressure, sustained duration, high pressure zone, defecation index, and coughing reflex were not significantly different between the two groups (Table 3). Similar trends were observed in subgroups of patients based on cancer location (mid or low rectal cancer), radiotherapy, and type of resection (ultra-low anterior resection and intersphincteric resection) (Table 4-6).

Table 3 Anorectal manometry measurements between groups

	Major incontinence (*n* = 92)	**Continent/minor incontinence (*n* = 81)**	***P***
Mean resting pressure, mmHg	28.4 ± 15.8	34.3 ± 18.6	0.027
Resting asymmetry, %	39.1 ± 11.7	34.1 ± 9.6	0.002
Max squeezing pressure, mmHg	117.3 ± 65.9	133.3 ± 65.5	0.111
Squeeze asymmetry, %	34.2 ± 9.3	31.4 ± 8.3	0.046
Sustained duration, s	35.2 ± 19.8	33.6 ± 23.5	0.632
Sphincter length, cm	3.3 ± 1.1	3.7 ± 1.0	0.034
High pressure zone, cm	2.2 ± 1.1	2.4 ± 0.9	0.160
Defecation index	1.7 ± 1.1	1.6 ± 1.1	0.507
Coughing reflex, %	134.6 ± 105.7	125.9 ± 74.6	0.543
Resting vector volume, $mmHg^2 \cdot mm$	143,601 ± 118,961	278,922 ± 289,674	<0.001

Values are expressed as the mean ± standard deviation

Table 4 Subgroup analysis of anorectal manometry according to cancer location

	Mid rectal cancer: 5–10 cm from anal verge (n=39)			**Low rectal cancer: <5 cm from anal verge (n=134)**		
	Major incontinence (n = 24)	Continent/minor incontinence (n = 15)	P	Major incontinence (n = 68)	Continent/minor incontinence (n = 66)	P
Mean resting pressure, mmHg	26.0 ± 14.8	28.7 ± 16.0	0.588	29.2 ± 16.2	35.6 ± 19.1	0.043
Resting asymmetry, %	37.4 ± 10.1	34.9 ± 8.6	0.447	39.7 ± 12.1	33.9 ± 9.8	0.003
Maximal squeezing pressure, mmHg	101.7 ± 52.4	130.6 ± 63.9	0.132	122.8 ± 69.5	133.9 ± 66.4	0.345
Squeeze asymmetry, %	35.1 ± 8.5	32.9 ± 11.3	0.485	33.8 ± 9.7	31.1 ± 7.5	0.073
Sustained duration, s	36.4 ± 18.7	44.3 ± 25.3	0.273	34.7 ± 20.3	31.1 ± 22.5	0.340
Sphincter length, cm	3.4 ± 1.0	3.3 ± 0.8	0.609	3.3 ± 1.1	3.8 ± 1.0	0.013
High pressure zone, cm	2.2 ± 1.1	2.1 ± 0.8	0.865	2.2 ± 1.0	2.5 ± 0.9	0.106
Defecation index	1.8 ± 1.4	1.6 ± 1.2	0.628	1.7 ± 1.0	1.6 ± 1.0	0.673
Coughing reflex, %	117.4 ± 63.8	146.5 ± 68.9	0.187	140.9 ± 117.2	121.1 ± 75.6	0.255
Resting vector volume, $mmHg^2 \cdot mm$	153,941 ± 127,846	227,082 ± 225,016	0.202	139,897 ± 116,401	290,704 ± 302,669	<0.001

Values are expressed as the mean ± standard deviation

Table 5 Subgroup analysis of anorectal manometry according to prior radiotherapy

	Radiotherapy (*n* = 122)			**No radiotherapy (*n* = 51)**		
	Major incontinence (*n* = 62)	Continent/minor incontinence (*n* = 60)	*P*	Major incontinence (*n* = 21)	Continent/minor incontinence (*n* = 30)	*P*
Mean resting pressure, mmHg	28.3 ± 15.2	34.5 ± 18.1	0.046	28.6 ± 17.2	33.8 ± 20.5	0.335
Resting asymmetry, %	39.5 ± 11.8	33.9 ± 9.8	0.005	38.3 ± 11.6	34.4 ± 9.2	0.205
Maximal squeezing pressure, mmHg	116.2 ± 66.6	131.1 ± 64.4	0.215	119.3 ± 65.4	139.6 ± 69.8	0.294
Squeeze asymmetry, %	33.5 ± 9.9	31.8 ± 7.2	0.268	35.5 ± 8.1	30.5 ± 10.9	0.068
Sustained duration, s	34.4 ± 20.6	36.0 ± 25.6	0.715	36.6 ± 18.4	26.3 ± 13.4	0.036
Sphincter length, cm	3.3 ± 1.1	3.6 ± 0.9	0.131	3.4 ± 0.9	3.9 ±1.2	0.103
High pressure zone, cm	2.1 ± 1.1	2.4 ± 0.9	0.149	2.3 ± 1.1	2.4 ± 0.9	0.710
Defecation index	1.6 ± 0.9	1.6 ± 1.0	0.874	2.0 ± 1.4	1.8 ± 1.2	0.587
Coughing reflex, %	140.7 ± 108.0	130.9 ± 77.4	0.570	122.4 ±101.6	110.8 ± 65.1	0.651
Resting vector volume, $mmHg^2 \cdot mm$	139,132 ± 128,678	261,808 ± 205,540	<0.001	152,688 ± 97,640	327,819 ± 455,660	0.046

Values are expressed as the mean ± standard deviation

Table 6 Subgroup analysis of anorectal manometry measurements according to type of resection

	Ultra-low anterior resection (*n* = 103)			**Intersphincteric resection (*n* = 48)**		
	Major incontinence (*n* = 49)	Continent/minor incontinence (*n* = 54)	*P*	Major incontinence (*n* = 27)	Continent/minor incontinence (*n* = 21)	*P*
Mean resting pressure, mmHg	30.7 ± 14.5	39.3 ± 17.5	0.009	24.7 ± 17.3	26.0 ± 18.1	0.796
Resting asymmetry, %	38.2 ± 10.4	32.1 ± 8.0	0.001	39.2 ± 14.5	36.1 ± 10.7	0.415
Maximal squeezing pressure, mmHg	124.4 ± 66.2	136.8 ± 64.6	0.338	104.7 ± 61.6	138.9 ± 69.9	0.079
Squeeze asymmetry, %	35.7 ± 9.6	30.7 ± 7.7	0.004	31.6 ± 9.7	31.2 ± 6.9	0.880
Sustained duration, s	35.8 ± 20.5	32.7 ± 22.2	0.459	34.2 ± 22.3	34.1 ± 26.1	0.984
Sphincter length, cm	3.4 ± 0.9	3.7 ± 1.0	0.180	3.2 ± 1.2	3.8 ±1.0	0.094
High pressure zone, cm	2.2 ± 1.1	2.4 ± 0.8	0.270	2.1 ± 1.0	2.4 ± 1.1	0.328
Defecation index	1.7 ± 1.0	1.5 ± 1.0	0.432	1.9 ± 1.0	1.8 ± 1.1	0.773
Coughing reflex, %	126.3 ± 79.5	133.8 ± 75.1	0.625	151.4 ± 143.6	100.9 ± 67.7	0.154
Resting vector volume, $mmHg^2 \cdot mm$	144,596 ± 118,226	314,855 ± 315,410	0.001	124,480 ± 101,217	206,844 ± 205,744	0.075

Values are expressed as the mean ± standard deviation

Multivariable analysis showed that resting vector volume was the only statistically significant variable for major incontinence (Table 7). Anorectal manometry parameters included in the multivariable analysis were mean resting pressure (P = 0.027), squeezing pressure (P = 0.111), asymmetry at rest (P = 0.002), asymmetry at squeezing (P = 0.046), sphincter length (P = 0.034), high pressure zone length (P = 0.160), and resting vector volume (P < 0.001). Because the vector volume is normally represented in the hundred–thousand-unit range, it was not possible to show an increased risk per unit increment in this parameter. Thus, a subsequent multivariable analysis was done by reducing the variable by a factor of 100,000 which yielded an odds ratio of 0.675 per 100,000 mmHg2•mm (95% confidence interval, 0.532–0.823; P = 0.006). The AUC for resting vector volume was 0.663. A cutoff value of 242,710 mmHg2•mm (decrease in vector volume increases severity) was obtained with a sensitivity of 84.8% and specificity of 50.6% by maximizing the Youden index (Fig. 4).

Table 7 Multivariable analysis of manometric parameters for major incontinence

	OR	**95% CI**	***P***
Mean resting pressure, per mmHg	1.009	0.985–1.035	0.456
Resting asymmetry, per %	1.022	0.979–1.066	0.324
Maximal squeezing pressure, per mmHg	0.999	0.993–1.004	0.589

Squeeze asymmetry, per %	1.022	0.979–1.066	0.324
Sphincter length, per cm	0.858	0.502–1.467	0.575
High pressure zone, per cm	1.223	0.716–2.088	0.462
Resting vector volume, per mmHg^2·mm	1.000	1.000–1.000	0.008

OR, hazard ratio; CI, confidence interval

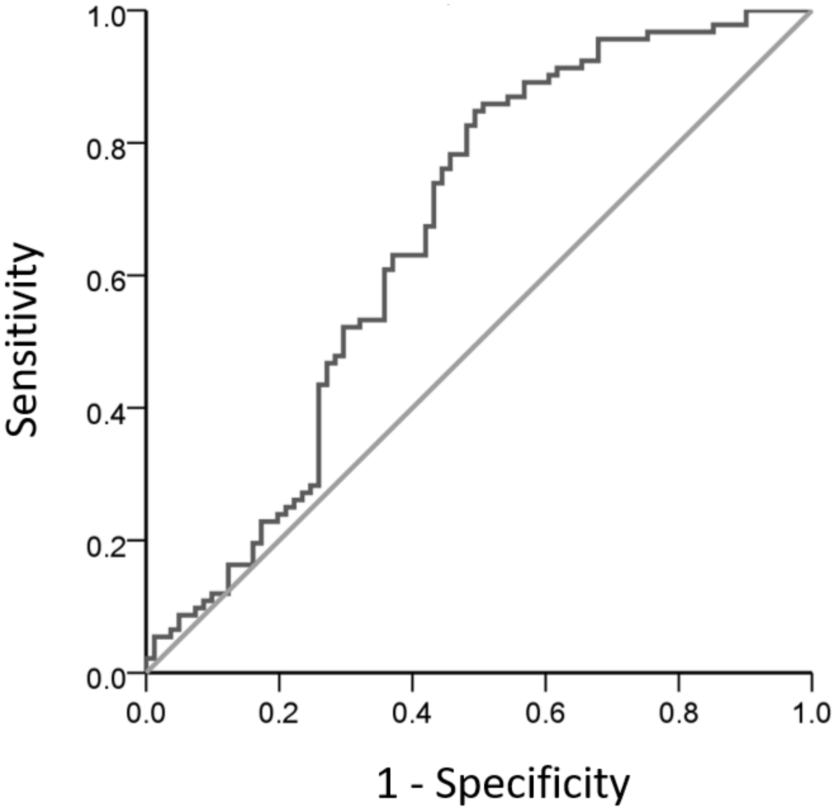


Fig. 4 Receiver-operating characteristic curve of resting vector volume for predicting major incontinence. Area under the curve = 0.663

Discussion

There is no definitive test before ileostomy reversal for predicting fecal incontinence, even though there is a high incidence of fecal incontinence following sphincter-preservation surgery that usually occurs after restoration of bowel continuity. This study suggests that a decreased resting vector volume shown on anorectal manometry performed before ileostomy reversal is associated with increased risk of major fecal incontinence after sphincter-preservation surgery. Using this cohort of patients, we determined a cutoff value for resting vector volume before ileostomy reversal as a predictor of major incontinence in patients with mid or low rectal cancer. This cutoff value should be validated in a well-designed large-scale study.

Fecal incontinence is a debilitating condition after sphincter-preservation surgery, with a significant negative impact on the patient's quality of life [6]. Although fecal incontinence usually improves during the first year after surgery [28], it may persist for longer, especially in patients with a low rectal tumor or those who undergo chemoradiotherapy [8]. The ability to predict which patients are at increased risk of fecal incontinence, before performing ileostomy reversal, would be helpful to patients because it may be possible to prevent fecal incontinence. Objective assessment of anal canal function before undergoing ileostomy reversal is a logical step towards providing the patient with better treatment options.

Many approaches have been used to investigate fecal incontinence, including diagnostic tests of sphincter morphology, nerve integrity, and function such as magnetic resonance imaging, endoscopic ultrasonography, pudendal nerve terminal latency test, and anorectal manometry. However, imaging alone does not provide adequate information about anal function, and results of the pudendal nerve terminal latency test were controversial [29]. We believe that anal manometry is the most direct method for assessing anal function. Although several studies have performed anorectal manometry after sphincter-preservation surgery in patients with fecal incontinence, few of these studies determined a cutoff value that could be used to predict fecal incontinence after ileostomy reversal, although changes in anal sphincter pressure, symmetry, and rectal compliance have been documented [10-15]. Thus, we need better understanding of the physiologic changes caused by structural defects of the anal sphincter following sphincter-preservation surgery. The present study showed that patients with major incontinence had lower resting pressure, greater asymmetry of the anal canal, and shorter sphincter length compared with the continent/minor incontinence group, as reported in previous studies [10-15]. Maximal squeezing pressure was not low in major incontinence, consistent with prior studies [10, 13-14]. Although reduced compliance of the neorectum and decreased sensitivity of the anus to propulsion forces were reported in prior studies [10, 13-15], we did not measure rectal compliance for safety concerns, such as the risk of rectal perforation during measurement [26].

Our study showed that the resting vector volume was inversely correlated with the severity of fecal incontinence. We believe the clinical relevance of resting vector volume was underestimated in the past compared to usual parameters such as pressure, asymmetry, or sphincter length and should be revisited. The anal canal is a three-dimensional structure and all of its components, including the muscles and nerves, act together to maintain continence. Therefore, a more comprehensive integrated parameter, such as resting vector volume, is better qualified to assess the overall quality of anal function and continence. The resting vector volume is calculated from three-dimensional profilometric pressure measurements across the anal sphincter at the resting state. The radial area of the pressure profile is calculated across each cross-section and integrated across the z-axis of the anal canal, resulting in a lower value if there is a loss of function of the internal anal sphincter in any segment or direction [27]. Previous studies showed that the resting vector volume after rectal surgery was generally lower in continent patients than in healthy individuals [14-15, 30]. We think that that decreases in sphincter length, resting pressure, or symmetry would result in a decreased resting vector volume, which will provide a better representation of the three-dimensional structural function of the anal canal.

In our study, we estimated a cutoff vector volume value of 242,710 mmHg2·mm for predicting major incontinence by maximizing the Youden index. However, the AUC of this curve was 0.663 and is a limitation to generalizing our findings. Lack of standardization of protocol and interpatient variablity has prevented wide-spread use of manometry parameters into daily clinical decision making [27]. We consider that the optimal cut-off value should be evaluated with consideration of interpatient variability as well as a standardized protocol to help clinical decision. Additional well-designed studies are needed to confirm the clinical value and cutoff value of resting vector volume as a predictor for major incontinence after sphincter-preservation surgery.

The proportion of patients suffering from fecal incontinence after sphincter-preservation surgery vary ranging from 0-71%, with an increased risk for low tumors and neoadjuvant radiotherapy [6, 8]. The high prevalence of fecal incontinence in our cohort is partly due to the fact that over 95% of rectal cancer patients underwent sphincter preservation surgery in our facility, which is one of the strengths of our study. There is a trend toward more sphincter-preservation surgeries being performed than in the past [31, 32], which subsequently will increase patients suffering from fecal incontinence. Additionally, in our cohort 72% of patients underwent neoadjuvant chemoradiotherapy and 77.5% of patients were low rectal tumors (within 5cm from anal verge), which also contributes to a higher risk of fecal incontinence.

Our study holds some limitations and unsolved issues to discuss.

First, the decision to undergo anorectal manometry testing and FISI questionnaire survey was not prospectively controlled, introducing the possibility of selection bias. The FISI questionnaire was not administered before primary surgery or more than 1 year after surgery. Thus, the effects of sphincter-preservation surgery on further deterioration of sphincter function and/or recovery are unknown. Additionally, the predictive ability of anorectal manometry was based on the assumption that anal function would be greatly unaltered after restoration of continuity. Functional recovery can occur to various degrees at various paces depending on the patient, which would have further contributed to the limitations to this study. Second, patients were not assessed for pelvic nerve function due to safety issues, thus whether incontinence was induced by nerve damage or structural defects is unknown. Third, we did not consider the possibility of age and sex differences in anal canal physiology because of the small number of patients. Future studies that account for these subgroup differences may yield differing results. Lastly, the generalizability of resting vector volume would be limited without a larger scale study. On subgroup analysis, although a trend was observed, some subgroups failed to show a statistically significant difference of the resting vector volume.

In conclusion, this study revealed that resting vector volume measured before ileostomy reversal may be a predictor of major incontinence in patients undergoing sphincter-preserving surgery for mid or low rectal cancer. We suggest that preoperative counseling should be offered to patients at increased risk of fecal incontinence, especially in patients with a low resting vector volume. We also suggest that the physiology of the anorectum should be discussed with patients before ileostomy reversal.

Disclosures

The authors have no conflict of interest to declare.

Ethical statement

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Institutional and National) and with the Helsinki Declaration of 1964 and later versions. (IRB No. B-1808-484-105)

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국문초록

연구배경: 변실금은 직장암환자에서 항문보존 수술 이후 자주 발생하는 합병증으로 알려져 있으나 장루복원수술 전에 이러한 변실금이 발생하는 것을 예측하는 인자는 잘 알려져 있지 않다. 고로 이 연구에서는 중/저위 직장암 환자에서 장루복원 수술 전에 항문내압검사를 시행함으로서 심한 변실금을 예측할 수 있는 인자들에 대하여 연구하였다.

연구방법: 이 연구는 전향적으로 수집되는 데이터베이스에서 추출한 후향적 연구이며 분당서울대학교병원에서 중/저위 직장암으로 수술 받고 장루복원수술을 받은 환자들 중 복원술 전 항문내압검사를 시행한 173명의 환자들을 대상으로 삼았다. 변실금의 정도 평가는 항문보존수술 후 1년째에 Fecal Incontinence Severity Index를 이용하였고 25점 이상인 심한 환자군과 그 이하인 환자들로 나누어 분석을 하였다. 항문내압검사에서 얻은 항목들을 통계적으로 분석하여 심한 변실금의 예측인자들을 분석하였다.

결과: 전체 환자들 중 92명 (53.1%)는 수술 후 1년 째 심한 변실금을 경험하였다. 심한 환자들과 그렇지 않은 양군간의 비교에서 암의 위치, 병기, 수술전 방사선요법의 비율 등은 차이가 없었으나 심한 변실금 환자들은 항문내압검사에서 더 낮은 휴식기 압력 (28.4 vs. 34.3 mmHg, $P = 0.027$), 더 큰 휴식기 비대칭성 (39.1% vs. 34.1%, $P = 0.002$)과 수축기 비대칭성 (34.2% vs. 31.4%, $P = 0.046$), 더 짧은 항문길이 (3.3 vs. 3.7 cm, $P = 0.034$), 그리고 더 작은 휴식기 벡터부피(resting vector volume, 143,601 vs. 278,922 $mmHg^2$•mm, $P < 0.001$)를 보였다. 이들 중 휴식기 벡터부피만이 심한 변실금의 예측인자로 확인되었다 (odds ratio = 0.675 per 100,000 $mmHg^2$•mm, 95% confidence interval, 0.532–0.823; $P = 0.006$)..

결론: 상기 결과를 보았을 때 장루복원수술 전 시행한 항문내압검사에서 휴식기 벡터부피는 심한 변실금의 예측인자가 될 수 있다는 것을 보여주었다. 항문내압검사를 통해 변실금이 발생할 위험이 높은 환자들은 항문의 이러한 생리/해부학적 변화에 대하여 장루복원수술을 시행하기 전 충분히 주지를 시켜주어야 한다.

주요어 : 항문내압검사, 장루복원수술, 변실금

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