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중하부 직장암 환자에서 영구장루형성의 예측인자 평가 : 수술전 항문기능에 대한 다기관 코호트연구

Predictors of permanent stoma creation in patients with mid or low rectal cancer: results of a multicentre cohort study with preoperative evaluation of anal function

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서울대학교 대학원
의학과 외과학 전공
김 성 환

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지도교수 강 성 범

이 논문을 의학석사 학위논문으로 제출함

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의학과 외과학 전공

김 성 환

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위 원 장 _____ (인)

부 위 원 장 _____ (인)

위 원 _____ (인)

Abstract

Predictors of permanent stoma creation in patients with mid or low rectal cancer: results of a multicentre cohort study with preoperative evaluation of anal function

Sunghwan Kim

Department of Medicine, Surgery

The Graduate School

Seoul National University

Aim: Preoperative factors predictive of permanent stoma creation were investigated in a long-term follow-up of patients with mid or low rectal cancer.

Methods: We included patients who underwent radical resection for

mid or low rectal cancer with available data for preoperative anal function measured by manometry and Faecal Incontinence Severity Index questionnaire between January 2005 and December 2015 in three tertiary referral hospitals. A permanent stoma was defined as a stoma present until the patient's last follow-up visit or death. Preoperative factors that predicted permanent stoma creation were analysed.

Results: Over a median follow-up of 57.4 months (range 12 - 143 months), a permanent stoma was created in 144/577 (25.0%) patients, including 89 (15.4%) who underwent abdominoperineal resection, one (0.2%) who underwent Hartmann's operation without reversal, 15 (2.6%) with a diverting ileostomy at the time of initial sphincter-preserving surgery without undergoing stoma reversal, and 39 (6.8%) who underwent permanent ileostomy formation after sphincter-preserving surgery. Patients with permanent stoma creation had a shorter tumour distance from the anal verge ($P < 0.001$), larger tumour size ($P = 0.020$) and higher preoperative Faecal Incontinence Severity Index score ($P = 0.020$). On multivariable analysis, tumour distance from the anal verge predicted permanent stoma formation (relative risk 0.53 per centimetre increase; 95% confidence interval 0.46 - 0.60; $P < 0.001$) but preoperative anal function did not.

Conclusion: Tumour distance from the anal verge was the only preoperative determinant of permanent stoma creation in rectal cancer patients. These data may help mid and low rectal cancer patients

understand the need for permanent stoma.

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Keywords : Rectal cancer; Faecal incontinence; Anal function; Permanent stoma; Abdominoperineal resection;

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Table of contents

I. Introduction

A permanent stoma may be created in patients with rectal cancer to ensure oncological safety or because of anorectal dysfunction, although a stoma may have a detrimental effect on the patient's quality of life[1]. A permanent stoma can be created during the patient's initial abdominoperineal excision (APR) or as a salvage procedure following sphincter-preserving surgery (SPS). The National Comprehensive Cancer Network guidelines for rectal cancer recommend performing APR if the tumour directly involves the anal sphincter or the levator muscles, or if margin-negative resection of the tumour would result in loss of anal sphincter function and incontinence[2]. However, neoadjuvant radiotherapy, age, tumour size and tumour distance from the anal verge have also been reported as predictors of APR[3-8]. In addition, comorbidities, surgical complications, anastomotic leakage and local recurrence are associated with the creation of a permanent stoma after SPS[9-23].

However, no studies have investigated whether preoperative anal function is a predictor of permanent stoma creation. Furthermore, prior studies focused on predictors of APR during initial surgery, or predictors for creating a permanent stoma as part of salvage therapy or a sustained temporary stoma after initial SPS. Therefore, we investigated the preoperative predictors, including quantitatively measured preoperative anal function, for permanent stoma creation in a long-term follow-up of patients with mid or low rectal cancer.

II. Methods

We performed this retrospective cohort study using a database of patients treated at the following tertiary referral hospitals in Korea: Seoul National University Bundang Hospital (SNUBH), the National Cancer Center (NCC) and Seoul National University Hospital (SNUH). Data were collected for patients with rectal cancer who underwent radical surgery, including APR with a curative intent, between January 2005 and December 2015. The inclusion criteria were as follows: histologically confirmed mid or low rectal adenocarcinoma located ≤ 10 cm from the anal verge; no previous colorectal surgery or malignancy; no evidence of distant metastasis at the time of surgery; Faecal Incontinence Severity Index (FISI) questionnaire[24] and anal manometry recorded preoperatively; and follow-up for more than 1 year after surgery. This study was approved by the ethical review boards at each institution (SNUBH, B-1710/429-105; SNUH, J-1801-004-911; NCC, NCC2018-0006).

We used standard neoadjuvant and/or adjuvant chemoradiotherapy regimens. Patients received a fluoropyrimidine- based chemoradiotherapeutic regimen. Long-course radiotherapy was performed with a total dose of 50.4 Gy, of which 45 Gy was applied in 25 fractions to the pelvis and a 5.4 Gy boost was applied in three fractions to the primary tumour over 5.5 weeks. Surgery was performed 6–8 weeks after the chemoradiotherapeutic regimen was completed. The surgical procedure, stoma creation and anastomosis

methods were chosen at the surgeon's discretion. Most surgeons preferred circular-stapled anastomosis or, if the rectal stump was too short, hand sewing was performed instead. APR was mainly performed if the surgeon thought that a free margin could not be obtained grossly or on frozen biopsy samples.

Demographic, perioperative and postoperative data were retrieved from the patients' medical records. Demographic data included age, sex, body mass index and American Society of Anesthesiologists class. Perioperative data included tumour distance from the anal verge, carcinoembryonic antigen (CEA) level, clinical stage, FISI questionnaire[24] and manometry data. For manometry, an eight-channel catheter was inserted into the anorectum, and the pressures in the anal canal were measured by a continuous pull-through technique at a speed of 0.5 mm/s[25]. The preoperative FISI questionnaire was completed after neoadjuvant therapy for patients receiving neoadjuvant therapy. Regarding tumour size, to reflect the difficulty of operation with respect to tumor size, we used the pathological tumour size, which was defined as the largest dimension of the pathological specimen. Tumours were staged according to the 7th edition of the American Joint Committee on Cancer staging system[26]. Tumour distance from the anal verge, clinical T stage and N stage were recorded before the start of neoadjuvant therapy.

All the patients were followed up according to our standard postoperative surveillance protocol for colorectal cancer. Postoperative information collected during this period included physical examinations,

serum CEA levels and CT findings. CT of the chest, abdomen and pelvis was performed every 6 months for the first 2 years and every 6 - 12 months for 3 years, until postoperative year 5. A permanent stoma was defined as a stoma created during initial surgery or created at a later time that remained until the patient's last follow-up visit or death. The decision to create a stoma during the follow- up period was at the surgeon's discretion if the patient agreed with the procedure.

Results are presented as proportions or as the mean and standard deviation depending on the type of variable. For continuous variables, means were compared using Student's t test. Categorical variables were analysed using Pearson's v2 or Fisher's exact test, as appropriate. Variables with P values of < 0.1 in univariable logistic regression analysis were included in multivariable logistic regression analysis. All statistical tests were two-sided. A P value of < 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS software for Windows, version 19.0 (SPSS Inc., Chicago, Illinois, USA).

III. Results

The patient demographics are shown in Table 1. The mean age of the patients was 59 ± 11 years. At initial rectal cancer surgery, 89 patients underwent APR and one patient underwent Hartmann's operation to create a permanent stoma. Of 487 patients who underwent

SPS, 444 patients underwent ileostomy and stoma reversal was not performed in 15 of these patients. Therefore, a permanent stoma was created during initial surgery in 105 patients. Of 472 patients without an initial stoma or patients who had already undergone stoma repair after initial surgery, a stoma was created in 39 patients and was classified as permanent. Accordingly, 144 patients had a permanent stoma in our cohort (Fig. 1).

The most common reason for creating a primary permanent stoma (i.e. APR or Hartmann's operation; 15.6% of the total cohort) was the initial location of the tumour followed by anal dysfunction. There were four patients with tumours located > 4 cm from the anal verge who underwent APR. All these patients had anal dysfunction (FISI score range 25 – 49; mean resting pressure range 9.5 – 51.9 mmHg). The reasons for secondary stoma formation were anastomotic complications (5.4%) followed by tumour recurrence (2.9%) and poor anal function (1.0%). The results are summarized in Fig. 2. Table 2 shows the stoma formation rates according to the hospitals. Figure 3 shows the cumulative incidence of permanent stoma creation in the entire cohort according to the aetiology. The median followup was 57.4 months (range 12 – 143 months). The incidence of permanent stoma creation at initial surgery was 18.2%. The cumulative incidence of stoma creation was 19.4% at 1 year after initial surgery and it increased gradually over time, reaching 24.8% at 5 years after initial surgery.

The results of univariate analysis of possible predictors of permanent stoma creation are shown in Table 2. A short tumour distance from

the anal verge, larger tumour size and higher preoperative FISI score were associated with permanent stoma creation. Multivariable analysis was performed on relevant factors with inclusion of age, sex and the clinical T and N stages. To check for potential confounding factors, we assessed whether the FISI score was correlated with tumour height but the correlation was poor (Pearson's r = −0.119, P = 0.004) and the R2 value was 0.014 in a linear regression model. We also examined the possibility of multicollinearity between the FISI score and potential confounding variables, including tumour distance, size and manometry parameters. However, we found no evidence of collinearity with the other variables included in the model (variance inflation factor 1.005 – 1.068). In multivariable analysis, tumour distance from the anal verge (OR 0.53; 95% CI 0.46 – 0.60; P < 0.001) was the only independent predictor of permanent stoma creation. Preoperative anal function was not associated with permanent stoma creation (OR 1.01; 95% CI 0.99 – 1.02; P = 0.42).

In subgroup analyses, we analysed the preoperative predictors of APR as initial surgery (Table 4) and the predictors of permanent stoma after SPS as initial surgery (Table 5). The rate of APR as initial surgery was 15.4% and the rate of permanent stoma creation after SPS was 11.3%. In both subgroup analyses, tumour distance from the anal verge was the only predictor of permanent stoma creation. In a subgroup analysis of patients with preoperative major faecal incontinence (FISI score IS25; n = 120)[27, 28] patients with a permanent stoma had lower tumours and lower squeezing pressures compared to

those without a permanent stoma (Table 6).

IV. Discussion

This study showed that tumour distance from the anal verge was the only independent predictor of permanent stoma creation in patients undergoing treatment for rectal cancer. Our hypothesis that preoperative anal function may be a predictor of permanent stoma was not proven in this study. To the best of our knowledge, this is the first study to evaluate whether preoperative markers of anal function, such as manometry and FISI scores, are potential predictors of permanent stoma creation.

The study considered the risk of permanent stoma throughout the treatment process, and defined permanent stoma as a stoma created during initial APR or at a later time, such as after SPS, by analysing long-term follow-up data. In our study, a permanent stoma was created in about one-quarter of patients with mid or low rectal cancer, which included patients who underwent APR as initial surgery (15.4%) and patients in whom a permanent stoma was created after SPS (11.3%). The APR rate was lower than that of previous studies, where it ranged from 23.4% to 41%[3-8].

Based on an analysis of risk factors for APR as initial surgery in a previous study, the decision to perform APR or SPS might represent the surgeon's preference, the quality of the hospital or surgical difficulty[4,7,8]. It is possible that patients were overlooked if a permanent

stoma was created after unnecessary SPS. In addition, the analysis of permanent stoma creation after SPS excluded patients who had already undergone APR, which may reduce the influence of preoperative risk factors for permanent stoma creation. Patients complaining of fecal incontinence with a high preoperative FISI score may increase surgeon's preference for APR. These trends are shown in the univariate analysis of Table 3. Therefore, we think that our decision to limit the univariable and multivariable analyses to preoperative factors allowed us to evaluate optimal predictors for the creation of a permanent stoma regardless of the type of treatment.

Our subgroup analyses showed that tumour distance from the anal verge was the only predictor of permanent stoma creation not only in APR as initial surgery but also after SPS as initial surgery. Postoperative factors, such as surgical complications and recurrence, were significant factors in prior studies evaluating permanent stoma after SPS[9–21], and tumour distance from the anal verge was a significant predictor of APR as initial surgery[3,4,6]. The fact that tumour distance is a predictor of permanent stoma after SPS in our study may be explained by prior findings that lower tumour height is associated with local recurrence[29] and surgical complications[30].

Although surgeons and patients generally prefer sphincter preservation, some patients may require permanent loop ileostomy or salvage stoma creation at a later date[9,12]. In this study, a defunctioning stoma was turned into a permanent stoma in 11.3% of patients, similar to the rates reported in previous studies[9,12]. In addition, the main cause

of subsequent stoma formation was anastomotic complications, such as leakage, stricture and ischaemic injury, similar to a recent meta-analysis of risk factors associated with nonclosure of dysfunctional stomas[9].

This study did not confirm that preoperative anal function, measured by manometry and FISI questionnaire, is a predictor of permanent stoma creation, even in the subgroup analyses of patients who underwent APR or SPS as initial surgery. This may reflect the complex physiology of the anorectum because its function may be preserved even in patients with low lying tumours, despite the tumour's proximity to the anal sphincter, but some dysfunction may occur owing to the bulk of the tumour or its invasion into surrounding tissues[31]. As such, FISI scores and manometry measurements did not show trends with tumour height and failed to show multicollinearity in the multivariable model. However, in a subgroup analysis of patients with preoperative major incontinence, patients with permanent stoma had lower tumours and lower squeezing pressures compared to those without permanent stoma. As shown in Figure 2, the proportion of patients with fecal incontinence sufficient to form a permanent stoma was small. Therefore, an increase in the number of enrolled patients would yield significant results. Further studies that focus on this cohort may provide answers in the future. Although our study did not show that preoperative anal function is a significant predictor conversion to permanent stoma after SPS[13,32].

Next, we discuss the limitations of our study. First, the retrospective

design may be subject to selective bias because patients complaining of defaecatory problemsprior to surgery were probably more likely to undergo functional assessment. A prospective study with routine preoperative evaluation of anorectal function may overcome this limitation. Second, the decision to perform APR or SPS was at the surgeon's discretion, and some surgeons may prefer APR, resulting in a difference in the proportion of APR. As such, there was a difference in the rate of primary colostomy and subsequent secondary stoma formation rates among the three centres. Third, a number of patients may have required secondary stoma formation but were censored due to lack of follow-up or death. Although 78% of patients without may not have been sufficient because five patients required secondary stoma formation more than 7 years after their primary surgery. Lastly, we only used four manometric parameters (resting pressure, squeezing pressure, sphincter length and high-pressure zone) from a range of parameters, which may introduce type II error. Some parameters, such as vector volume[33,34], sustained duration and rectoanal inhibitory reflex, were not measured in all patients due to differences in the protocols and software capabilities between each hospital.

This cohort study showed that tumour distance from the anal verge is the only preoperative determinant of permanent stoma creation in patients with rectal cancer. These data may help mid and low rectal cancer patients understand the need for permanent stoma better. The limitations of this retrospective study should be overcome in large, prospective cohort studies to reappraise the role of preoperative anal

function as a potential preoperative predictor for permanent stoma creation in patients with rectal cancer.

V. References

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Table 1. Baseline characteristics of total cohort and comparison of permanent vs. non-permanent stoma formation groups

	Total cohort (n = 577)	Comparison		
		Permanent stoma (n = 144)	No permanent stoma (n = 433)	p*
Age, years	58.8 ± 10.6	58.8 ± 11.3	58.8 ± 10.4	0.946
Sex, male	378 (65.5)	102 (70.8)	276 (63.7)	0.130
BMI ≥25 kg/m^2	213 (36.9)	48 (33.3)	165 (38.1)	0.320
ASA class				0.940
I	194 (33.7)	48 (33.3)	146 (33.9)	
II	367 (63.8)	93 (64.6)	274 (63.6)	
III	14 (2.4)	3 (2.1)	11 (2.6)	
Tumour distance from anal verge, cm	4.6 ± 2.3	2.7 ± 2.0	5.2 ± 2.1	<0.001
Tumour size, cm	2.3 ± 1.9	2.6 ± 1.9	2.2 ±1.9	0.020
CEA, ng/mL	4.7 ± 11.1	4.9 ± 12.3	4.6 ± 10.6	0.840
Clinical T stage				0.466
1	7 (1.2)	2 (1.4)	5 (1.2)	
2	50 (8.7)	10 (6.9)	40 (9.2)	
3	489 (84.7)	121 (84.0)	368 (85.0)	
4	31 (5.4)	11 (7.6)	20 (4.6)	
Clinical N stage				0.548
0	207 (35.9)	55 (38.2)	152 (35.1)	
1, 2	370 (64.1)	89 (61.8)	271 (64.9)	
FISI score	11.6 ± 15.0	14.3 ± 15.8	10.8 ± 14.7	0.016
Anorectal manometry measurements				

MRP, mmHg	50 ± 34	53 ± 34	49 ± 34	0.290
MSP, mmHg	143 ± 82	139 ± 82	144 ± 82	0.570
Sphincter length, cm	4.0 ± 1.1	3.9 ± 1.1	4.0 ± 1.1	0.640
High-pressure zone, cm	2.2 ± 0.9	2.2 ± 0.9	2.2 ± 0.9	0.820
Neoadjuvant chemoradiotherapy	500 (86.7)	129 (89.6)	371 (85.7)	0.260
Operation				<0.001
Low anterior resection	205 (35.5)	16 (11.1)	189 (43.6)	
Ultralow anterior resection	282 (48.9)	38 (26.4)	244 (56.3)	
Hartmann's operation	1 (0.2)	1 (0.7)	0	
Miles' operation	89 (15.4)	89 (61.8)	0	
Approach				0.001
Laparoscopy	359 (62.2)	73 (50.7)	286 (66.1)	
Open	218 (37.8)	71 (49.3)	147 (33.9)	

Values are reported as n (%) or mean ± standard deviation.
ASA, American Society of Anesthesiologists; BMI, body mass index; CEA, carcinoembryonic antigen; FISI, Faecal Incontinence Severity Index; MRP, mean resting pressure; MSP, maximal squeezing pressure.
*P-values for comparisons between the permanent and non-permanent stoma groups.

Table 2. Comparison of permanent stoma rates between treatment centres.

	Hospital #1 (*n* = 64)	Hospital #2 (*n* = 240)	Hospital #3 (*n* = 273)	*p*
Stoma formation				0.001
No stoma	40 (62.5)	181 (75.4)	212 (77.7)	
Stoma formation				
Primary colostomy	21 (32.8)	31 (12.9)	38 (13.9)	
Secondary stoma/ non-repaired stoma	3 (4.7)	28 (11.7)	23 (8.4)	

Table 3. Univariable and multivariable analyses of predictors of permanent stoma creation

	Univariable			Multivariable		
	RR	95% CI	*p*	RR	95% CI	*p*
Age						
<65 years	Ref			Ref		
≥65 years	1.00	0.67 - 1.50	0.986	1.10	0.69 - 1.76	0.701
Sex						
Male	Ref			Ref		
Female	0.72	0.48 - 1.09	0.122	0.68	0.42 - 1.09	0.112
BMI						
BMI <25 kg/m^2	Ref					
BMI ≥25 kg/m^2	0.81	0.55 - 1.21	0.304			
ASA class						
I, II	Ref					
III	0.81	0.22 - 2.96	0.755			
Tumour distance from anal verge, per cm	0.53	0.47 - 0.60	<0.001	0.53	0.46 - 0.60	<0.001
Tumour size, per cm	1.11	1.01 - 1.22	0.024	1.12	1.00 - 1.27	0.056
CEA, per ng/mL	1.00	0.99 - 1.02	0.837			
Clinical T stage						
1, 2, 3	Ref			Ref		
4	1.71	0.80 - 3.66	0.168	1.22	0.48 - 3.10	0.672
Clinical N stage						
0	Ref			Ref		
1, 2	0.88	0.59 - 1.29	0.503	0.91	0.56 - 1.46	0.680

FISI score	1.02	1.00 - 1.03	0.016	1.01	0.99 - 1.02	0.416
Anorectal manometry measurements						
MRP, per mmHg	1.00	1.00 - 1.01	0.294			
MSP, per mmHg	1.00	1.00 - 1.00	0.569			
Sphincter length, per cm	0.96	0.81 - 1.14	0.638			
HPZ, per cm	0.98	0.79 - 1.21	0.829			
Neoadjuvant chemoradiotherapy	1.44	0.79 - 2.62	0.235			

ASA, American Society of Anesthesiologists; BMI, body mass index; CEA, carcinoembryonic antigen; FISI, Faecal incontinence severity index; HPZ, high-pressure zone; MRP, mean resting pressure; MSP, maximal squeezing pressure; Ref: reference; RR: relative risk.

Table 4. Subgroup analysis of predictors of abdominoperineal resection (n = 89)

	Univariable			Multivariable		
	RR	95% CI	*p*	RR	95% CI	*p*
Age						
<65 years	Ref			Ref		
≥65 years	1.15	0.72 - 1.85	0.560	1.47	0.77 - 2.82	0.242
Sex						
Male	Ref			Ref		
Female	0.94	0.56 - 1.46	0.681	0.90	0.48 - 1.70	0.745
BMI						
BMI <25 kg/m^2	Ref					
BMI ≥25 kg/m^2	0.66	0.41 - 1.09	0.103			
ASA class						
I, II	Ref					
III	1.51	0.41 - 5.52	0.534			
Tumour distance from anal verge, per cm	0.31	0.24 - 0.39	<0.001	0.30	0.12 - 0.39	<0.001
Tumour size, per cm	1.10	0.99 - 1.23	0.076	1.11	0.94 - 1.31	0.216
CEA, per ng/mL	1.00	0.97 - 1.02	0.706			
Clinical T stage						
1, 2, 3	Ref			Ref		
4	2.38	1.06 - 5.36	0.036	2.01	0.59 - 6.80	0.261

Clinical N stage						
0	Ref			Ref		
1, 2	0.64	0.40 - 1.01	0.054	0.59	0.31 - 1.12	0.107
FISI score	1.02	1.01 - 1.04	0.003	1.02	1.00 - 1.04	0.054
Anorectal manometry measurements						
MRP, per mmHg	1.00	1.00 - 1.01	0.773			
MSP, per mmHg	1.00	1.00 - 1.00	0.378			
Sphincter length, per cm	0.96	0.78 - 1.18	0.692			
HPZ, per cm	0.90	0.69 - 1.17	0.421			
Neoadjuvant chemoradiotherapy	1.11	0.56 - 2.19	0.766			

ASA, American Society of Anesthesiologists; BMI, body mass index; CEA, carcinoembryonic antigen; FISI, faecal incontinence severity index; HPZ, high-pressure zone; MRP, mean resting pressure; MSP, maximal squeezing pressure; Ref, reference; RR, relative risk.

Table 5. Subgroup analysis of predictors of permanent stoma creation (n = 55) after sphincter-preserving surgery (n = 488)

	Univariable			Multivariable		
	RR	95% CI	*p*	RR	95% CI	*p*
Age						
<65 years	Ref			Ref		
≥65 years	0.82	0.45 - 1.52	0.536	0.96	0.51 - 1.81	0.893
Sex						
Male	Ref			Ref		
Female	0.54	0.28 - 1.05	0.067	0.54	0.28 - 1.04	0.066
BMI						
BMI <25 kg/m^2	Ref					
BMI ≥25 kg/m^2	1.08	0.61 - 1.92	0.786			
ASA class						
I, II	Ref					
III	N/A					
Tumour distance from anal verge, per cm	0.78	0.67 - 0.90	0.001	0.77	0.66 - 0.90	0.001
Tumour size, per cm	1.10	0.96 - 1.26	0.158	1.12	0.97 - 1.30	0.139
CEA, per ng/mL	1.01	0.99 - 1.03	0.476			
Clinical T stage						
1, 2, 3	Ref			Ref		
4	1.78	0.18 - 3.43	0.741	0.64	0.14 - 2.97	0.565

Clinical N stage						
0	Ref			Ref		
1, 2	1.44	0.77 - 2.70	0.251	1.40	0.73 - 2.67	0.316
FISI score	1.00	0.99 - 1.02	0.743	1.00	0.97 - 1.02	0.618
Anorectal manometry measurements						
MRP, per mmHg	1.01	1.00 - 1.01	0.218			
MSP, per mmHg	1.00	1.00 - 1.00	0.901			
Sphincter length, per cm	0.96	0.74 - 1.26	0.789			
HPZ, per cm	1.09	0.81 - 1.48	0.578			
Neoadjuvant chemoradiotherapy	2.13	0.74 - 6.11	0.159			

ASA, American Society of Anesthesiologists; BMI, body mass index; CEA, carcinoembryonic antigen; FISI, faecal incontinence severity index; HPZ, high-pressure zone; MRP, mean resting pressure; MSP, maximal squeezing pressure; Ref, reference; RR, relative risk.

Table 6. Comparison of baseline characteristics between permanent vs. non-permanent stoma formation groups for patients with pre-operative major incontinence (FISI ≥ 25)

	Permanent stoma (n = 38)	No permanent stoma (n = 82)	*p*
Age, years	60.1 ± 13.1	59.0 ± 11.0	0.635
Sex, male	27 (71.1)	54 (65.9)	0.677
BMI ≥25kg/m2	10 (26.3)	25 (30.5)	0.673
ASA class			0.739
I	14 (36.8)	33 (40.7)	
II	23 (60.5)	44 (54.3)	
III	1 (2.6)	4 (4.9)	
Tumour distance from anal verge, cm	2.8 ± 1.8	4.9 ± 1.9	<0.001
Tumour size, cm	3.1 ± 2.5	2.8 ± 2.3	0.418
CEA, ng/mL	3.3 ± 3.0	5.3 ± 8.4	0.157
Clinical T stage			0.249
1	0	0	
2	5 (13.2)	6 (7.3)	
3	27 (71.1)	69 (84.1)	
4	6 (15.8)	7 (7.5)	
Clinical N stage			1.000
0	8 (21.1)	18 (22.0)	

1, 2	30	(78.9)	64	(78.0)	
FISI score	36.7	± 9.9	36.4	± 9.6	0.887
Anorectal manometry measurements					
MRP, mmHg	37	± 21	47	± 33	0.100
MSP, mmHg	107	± 65	142	± 78	0.020
Sphincter length, cm	3.6	± 1.0	3.8	± 1.0	0.501
High-pressure zone, cm	2.0	± 0.7	2.3	± 1.0	0.099
Neoadjuvant chemoradiotherapy	34	(89.5)	62	(75.6)	0.090
Operation					<0.001
Low anterior resection	1	(2.6)	21	(25.6)	
Ultralow anterior resection	11	(28.9)	61	(74.3)	
Hartmann's operation	1	(2.6)	0		
Miles' operation	25	(65.8)	0		
Approach					0.326
Laparoscopy	17	(44.7)	46	(56.1)	
Open	21	(55.3)	36	(43.9)	

ASA, American Society of Anesthesiologists; BMI, body mass index; CEA, carcinoembryonic antigen; FISI, faecal incontinence severity index; HPZ, high-pressure zone; MRP, mean resting pressure; MSP, maximal squeezing pressure; Ref, reference; RR, relative risk.

Figure 1. Patient disposition. APR, abdominoperineal resection; Re-stoma, stoma recreation; SPS, sphincterpreserving surgery.

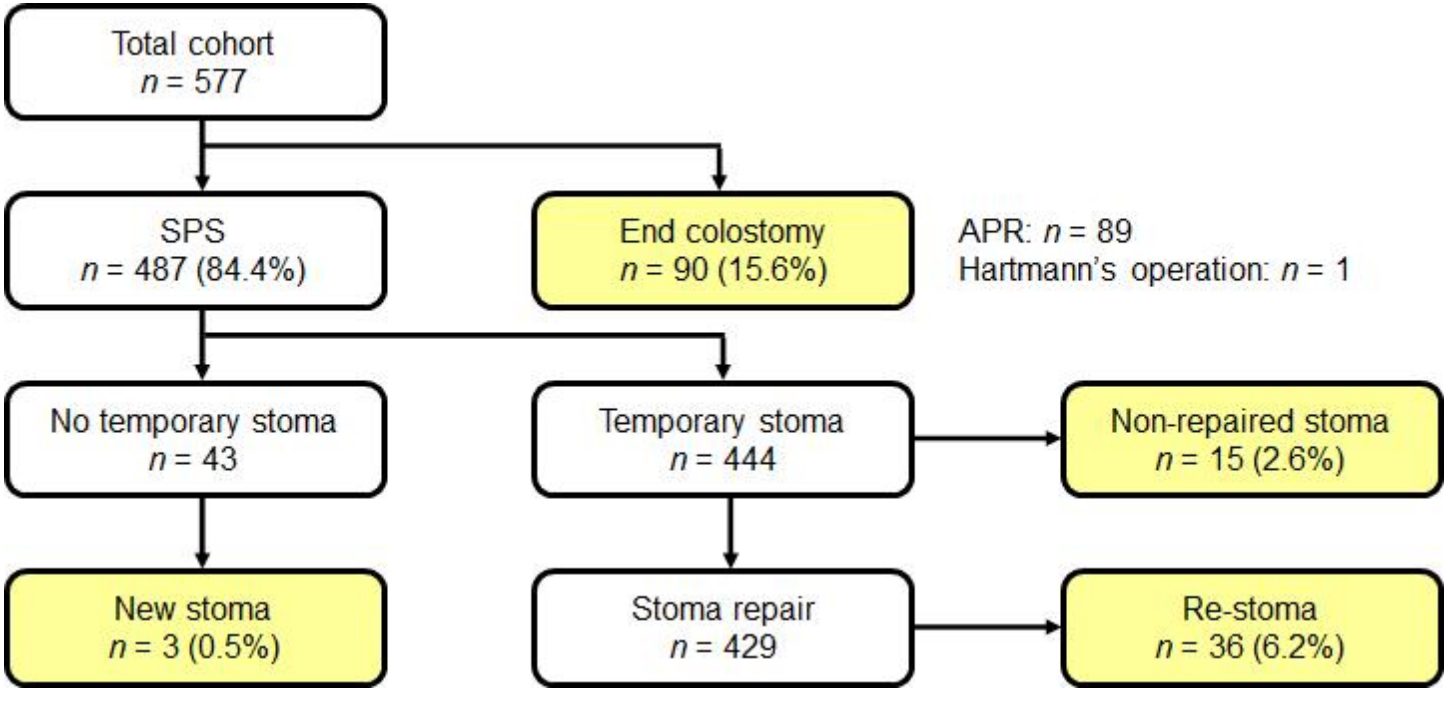


Figure 2. Aetiology of permanent stoma.

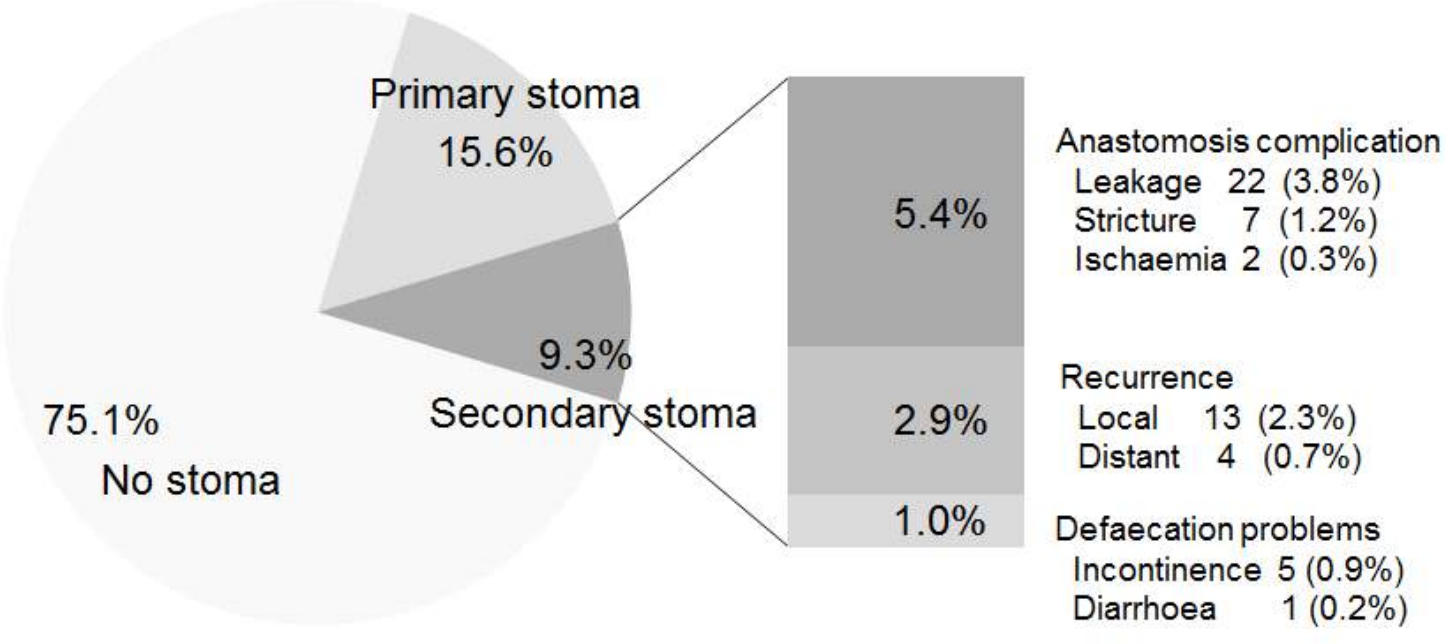
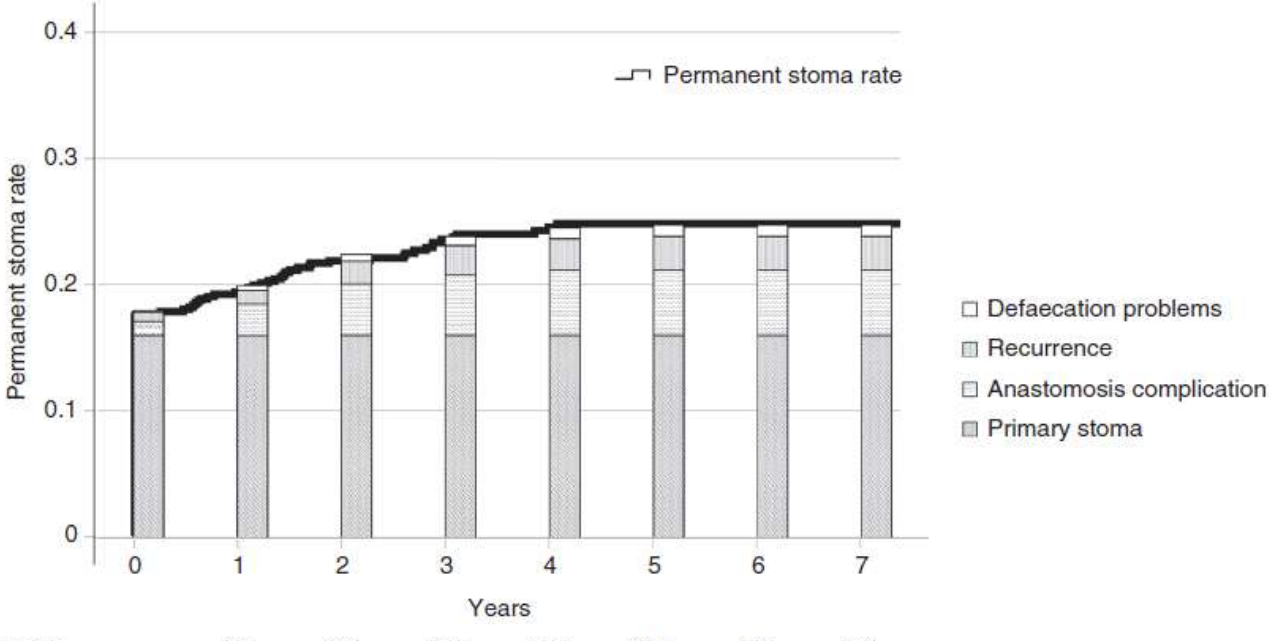


Figure 3. Kaplan–Meier plot of the cumulative incidence of permanent stoma creation from initial surgery according to aetiology.



국문초록

중하부 직장암 환자에서 영구장루형성의 예측인자 평가 : 수술전 항문기능에 대한 다기관 코호트연구

목적: 중하부 직장암 환자를 대상으로 장기간 추적관찰하여 영구적인 장루 생성을 예측할 수 있는 수술 전 요인을 알아보고자 하였다.

방법: 2005년 1월부터 2015년 12월까지 3개 3차 병원에서, 수술전 '항문압력검사'와 '변실금 중증도 지수 설문지'를 통해 항문 기능에 대한 데이터가 있는 중하부 직장암 환자 중 근치적 절제술을 시행한 환자를 포함했다. 영구 장루는 환자가 마지막으로 방문하거나 사망할 때까지 존재하는 장루로 정의되었다. 영구적인 장루 생성을 예측하는 인자를 수술 전 요인을 이용하여 분석하였다.

결과: 중앙값 57.4개월(12-143개월)의 추적 기간 동안 144/577(25.0%)의 환자에서 영구 장루가 생성되었으며, 이는 첫 수술에서 복회음절제술을 받은 89명(15.4%), 하트만수술을 받은 1명(0.2%)이 포함되었으며, 일시적 장루를 형성했다가 복원하지 못한 15명(2.6%), 첫 수술이후 장루를 다시 형성한 39명(6.8%)을 포함한다. 영구 장루 생성 환자는 항문 가장자리에서 더 짧은 종양 거리($P < 0.001$), 더 큰 종양 크기($P = 0.024$) 및 더 높은 수술 전 변실금 중증도 지수 점수($P = 0.016$)를 보였다. 다변량 분석에서 항문연부터 종양까지 거리는 영구적인 장루 형성을 예측했지만 (상대위험도 0.53/cm; 95% 신뢰 구간 0.46 - 0.60; $P < 0.001$), 수술 전 항문 기능은 통계적으로 유의하지 않았다.

결론: 직장암 환자에서 항문연부터 종양까지 거리는 수술 전 영구적인 장

루 생성을 결정하는 유일한 요인이었다. 이러한 데이터는 중하부 직장암 환자가 영구 장루의 필요성을 이해하는 데 도움이 될 수 있다.

주요어 : 직장암, 변실금, 항문기능, 영구장루, 복회음절제술
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