Table 2. Significance of subgrouping of tumour budding grade in high-grade tumour budding cases

Variables		Severe budding ($n = 32$)	Moderate budding ($n = 41$)	*P*-value
Mucinous/ signet-ring cell carcinoma	Yes	2 (18%)	9	0.099
	No	30 (48%)	32	
Medullary carcinoma	Yes	3 (50%)	3	0.99
	No	29 (43%)	38	
Node metastasis	Negative	12 (35%)	22	0.14
	Positive	20 (53%)	18	
Vessel invasion	Negative	2 (11%)	17	0.0009
	Positive	30 (56%)	24	
Growth pattern	Expanding	11 (30%)	26	0.014
	Infiltrating	21 (58%)	15	
Peritumoral lymphocytic infiltration	Present	5 (33%)	10	0.36
	Absent	27 (47%)	31	
Cytoplasmic pseudo-fragments	Low-grade	7 (30%)	16	0.12
	High-grade	25 (50%)	25	
β-catenin	Negative	13 (37%)	22	0.27
	Positive	19 (50%)	19	
LN-5γ2	Negative	11 (46%)	13	0.81
	Positive	21 (43%)	28	

tumoral lymphocytic infiltration ($P = 0.0077$) and negatively associated with a medullary growth pattern ($P = 0.011$). Unlike severe budding, cytoplasmic pseudo-fragments were associated with aberrant expression of both β-catenin ($P = 0.045$) and, more strikingly, LN-5γ2 ($P < 0.0001$) (Figure 3). Finally, there was no relationship between severe budding and cytoplasmic pseudo-fragments ($P = 0.12$) (Table 3).

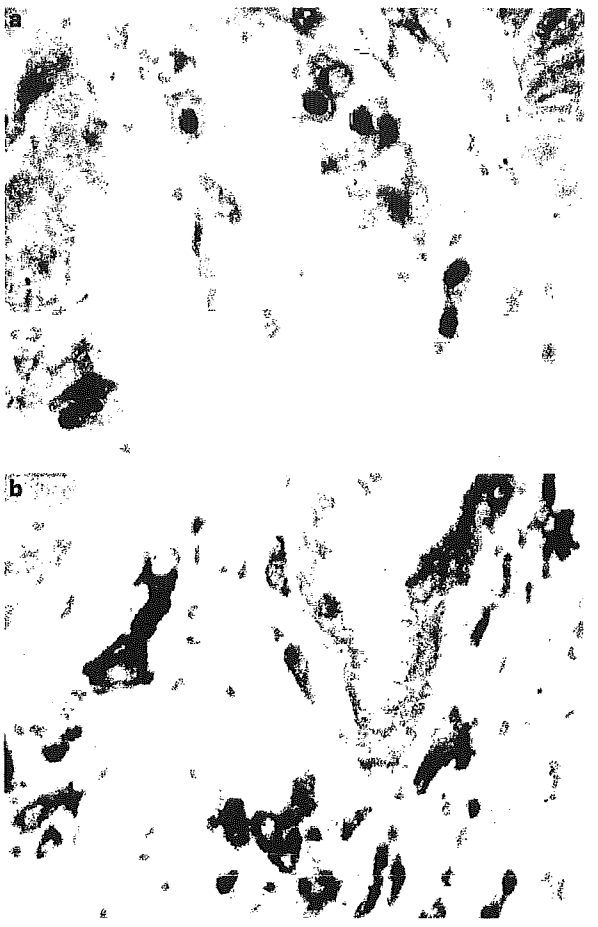

Figure 3. Microscopic appearance of the invasive front with immunostaining for β-catenin, and laminin-5 γ2 chain (LN-5γ2). In (a), β-catenin is positive in the nuclei of cancer cells composing tumour buds. In (b), LN-5γ2 is strongly positive in the cytoplasm of cancer cells forming tumour budding or forming cytoplasmic pseudo-fragments.

Discussion

There is good evidence that tumour budding is an important and independent prognostic factor in CRC.[1–4] In this study, we document a new feature strongly associated with tumour budding: cytoplasmic pseudo-fragments in the stroma surrounding budding foci. Serial section analysis indicated that cytoplasmic pseudo-fragments did not represent isolated cellular debris but were dendritic processes or pseudopodia extending from cancer cells. When 73 CRCs with high-grade budding were stratified on the basis of extent of budding (moderate versus severe) and presence of cytoplasmic pseudo-fragments, these features showed different relationships with established prognostic markers. Specifically, severe budding was strongly associated with vascular invasion, while cytoplasmic pseudo-fragments were strongly associated with diffuse infiltration, absent peritumoral lymphocytic infiltration and expression of LN-5γ2 by tumour cells. Importantly, there was no relation between extent of budding (within CRCs showing high-grade budding) and cytoplasmic pseudo-fragments. Together, these findings

Variables		Cytoplasmic pseudo-fragments high-grade ($n = 50$)	Cytoplasmic pseudo-fragments low-grade ($n = 23$)	P-value
Mucinous/signet-ring cell carcinoma	Yes	5 (45%)	6	0.074
	No	45 (73%)	17	
Medullary carcinoma	Yes	1 (17%)	5	0.011
	No	49 (73%)	18	
Node metastasis	Negative	21 (62%)	13	0.18
	Positive	29 (76%)	9	
Vessel invasion	Negative	9 (47%)	10	0.021
	Positive	41 (76%)	13	
Growth pattern	Expanding	19 (51%)	18	0.0014
	Infiltrating	31 (86%)	5	
Peritumoral lymphocytic infiltration	Present	6 (40%)	9	0.0077
	Absent	44 (76%)	14	
Tumour budding	Moderate	25 (61%)	16	0.12
	Severe	25 (78%)	7	
β-catenin	Negative	20 (57%)	15	0.045
	Positive	30 (79%)	8	
LN-5γ2	Negative	9 (38%)	15	0.0001
	Positive	41 (84%)	8	

Table 3. Significance of cytoplasmic pseudo-fragments in high-grade tumour budding cases

indicate that the extent of budding and cytoplasmic pseudo-fragments are not only independent prognostic markers but are indicative of different mechanisms of tumour aggressiveness. We speculate that the extent of tumour budding is an index of tumour cell discohesion, while cytoplasmic pseudo-fragments are a marker of a more dynamic interaction between cancer cells and host tissue. This is supported by the remarkably strong correlation between cytoplasmic pseudo-fragments and expression of LN-5γ2. If the extent of budding and cytoplasmic pseudo-fragments are independent markers of invasiveness, then the combination of the two may provide a very strong indication of tumour aggressiveness.

Experimental approaches using cells in culture have shown that Wnt signalling pathway activation promotes aggressive cytoplasmic transformation through an epithelial–mesenchymal transition to arborizing cells with filopodia.[17,18] In addition to the findings in serial sections, cytoplasmic pseudo-fragments were negatively associated with peritumoral inflammation that could trigger apoptosis. We therefore suggest that these structures characterize dendritic cell forms that are in a state of activation involving cell attachment and cell movement at the invasive tumour margin.

There were six medullary carcinomas with high-grade budding, but only one of these had cytoplasmic pseudo-fragments ($P = 0.011$). The lack of cytoplasmic pseudo-fragments is associated with the good prognosis of medullary carcinoma, particularly when the feature of DNA microsatellite instability (MSI) is present.[19] Dysregulation of the Wnt signalling pathway occurs less frequently in CRCs with MSI.[20] This would explain why the extent of budding was not related to expression of either β-catenin or LN-5γ2. That is, forms of budding that result from loss of cell cohesion, without additional activation of invasiveness, may be less dependent on Wnt pathway dysregulation. The relation between cytoplasmic pseudo-fragments and MSI status will be the subject of an additional report.

In summary, we suggest that tumour budding involves two processes that are largely independent. These are loss of cellular cohesion and cellular activation leading to increased invasiveness. The latter process is associated with the finding of cytoplasmic pseudo-fragments and is more dependent on dysregulation of the Wnt signalling pathway. However, the full adverse prognostic significance of tumour budding arises through the summation of cellular discohesion and increased invasiveness that generates a highly aggressive tumour phenotype.

Acknowledgements

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Surgical outcomes research

Long-term outcomes of a neo-anus with a pudendal nerve anastomosis contemporaneously reconstructed with an abdominoperineal excision of the rectum

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Background. *Pudendal nerve innervation can transform a neo-sphincter into an original anal sphincter–like muscle in animal studies. The results led us to clinical trials of a neo-anus with a pudendal nerve anastomosis (NAPNA). No long-term results in a series have been reported.*
Methods. *From 1995 to 2003, a neo-anus was reconstructed by using an inferior portion of the gluteus maximum muscle with a pudendal nerve anastomosis contemporaneously with an abdominoperineal excision of the rectum (APER) in 19 patients (17 men, 2 women; median age, 62.0 years; range, 46-73) with low-lying malignancy. The long-term (<2 years) clinical results were evaluated.*
Results. *The neo-sphincter began contracting (n = 15) at 6.6 ± 1.8 months after surgery; then the ileostomy was closed (n = 14) at 9.1 ± 2.6 months. The long-term results were studied in 10 patients (40.9 ± 14.1 months after ileostomy closure). All patients (100%) defecated at 4.8 ± 2.6 times/day without irrigation. Pads were used every day in 9 patients (90%). The Cleveland Clinic Florida incontinence score was 12.2 ± 3.3 points. No patients lost their occupation. Eight patients (80%) answered that their life with a NAPNA was better than with an ileostomy. The average World Health Organization Quality of Life-BREF in patients with NAPNAs was significantly better than that in those patients who underwent conventional APERs in our hospital (n = 27, 66.4 ± 0.8 years old) (P = .0402). Four patients (40%) experiencing the need to defecate got significantly better continence score (mean ± SD).*
Conclusions. *The sensitivity to recognize the need to defecate may be a key to success in NAPNAs. A NAPNA can be a practical option for selected patients wishing to avoid a stoma after an APER (Surgery 2005;137:8-15.)*

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DESPITE THE TECHNICAL ADVANCEMENT of bowel anastomosis in the lower rectum, the abdominoperineal excision of the rectum (APER) is now being performed in patients with very low-lying malignancies. The resulting stoma distorts the patient's body image[1] and worsens the quality of life (QOL).[2,3]

The neo-anus after APER has been recently reconstructed by using electrical stimulation of the neo-sphincter(s).[4-6] Although electric stimulation can create a neo-anal sphincter of sufficient strength and the electrically stimulated neo-sphincter has been reported to be effective in patients with fecal incontinence,[7-10] the clinical results after APER have been rather disappointing thus far.[5,6,10-12] These results may have been due to

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hepatocyte compartments. Studies for laboratory-grown kidneys are also underway with a similar approach at our laboratory but remain in their early phase.

CONCLUSION

Although tremendous progress and encouraging results have been achieved in the field of tissue engineering, many challenges remain and much work still needs to be done. The ultimate goal of tissue engineering is not only to replace structures and improve the function of diseased tissue, but also to build neo-organs for patients in need. Recent advances in stem cell biology, gene therapy, and engineering technology have allowed an extremely close interdisciplinary collaboration among developmental and cellular molecular biologists, gene therapists, materials engineers, chemists, and physicians, to move the laboratory-grown tissue and organ to clinical application.

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the following factors: The neo-sphincter could not voluntarily contract and relax in accordance with defecation, and/or there were no receptor mechanism to sense the need to defecate despite continuous contraction of the neo-sphincter on electrical stimulation.

The anal sphincter normally serves 3 important functions in controlling defecation: voluntary contraction and relaxation in accordance with defecation signals from the nervous system,[13] tonic activity in the resting state,[14] and a receptor mechanism to sense the need to defecate.[15] All 3 of these functions are controlled by the pudendal nerve and are theoretically necessary to achieve fecal continence in patients after a complete excision of defecation control system or APER. We have developed a new reconstructive procedure of a neo-anus with a pudendal nerve anastomosis (NAPNA). The primary concept underlying NAPNA is a nerve anastomosis between the pudendal nerve and a nerve innervating the neo-anal sphincter so as to accomplish the functions of the original anal sphincter. Both animal research[16] and simulated operations on human cadavers[17] led us to our clinical application.[18,19] This study reports the long-term outcomes in a series of patients with NAPNA who underwent contemporaneous reconstructions with APER.

PATIENTS AND METHODS

Patients with a NAPNA. Nineteen patients (17 men, 2 women; median age, 62.0 years; range, 46-73) with rectal carcinoma (n = 18; Dukes' classification A, 3 patients; Dukes' B, 8 patients; Dukes' C, 7 patients) and with a gastrointestinal stromal tumor (n = 1) underwent a NAPNA contemporaneously with an APER between February 1995 and January 2003. The median follow-up period was 38 months (range, 10-99 months) after surgery. The long-term outcomes were studied in 10 patients in which the period of neo-anus use exceeded 2 years compared to patients who had undergone conventional APERs.

Patients after a conventional APER. Fifty-three patients underwent conventional APERs in our hospital during the same period (from 1995 to 2000). The reasons for choosing conventional APERs are indicated in Table I. Because15 patients had died and 4 were terminally ill, we sent the other 34 patients the World Health Organization Quality of Life-BREF (WHOQOL-BREF) by mail. Twenty-seven (79.4%) patients (18 men, 9 women; median, 67 years old; range, 42-83; Dukes' A, 9 patients; Dukes' B, 10 patients; Dukes' C, 7 patients; Dukes' D, 1 patient) replied to the WHOQOL-BREF. Six patients did not answer the questionnaire because of dementia (n = 3) and for unclear reasons (n = 3).

Table I. Reasons why a NAPNA was not reconstructed in 53 patients after APER

Number of patients	*Reason*
19	severe local invasion and/or lymph node metastasis of rectal cancer
16	age older than 75
12	previous and/or supervened illness
6	metastasis to other organ,
4	introduced case to surgeons beyond our control
4	local recurrence of previous rectal cancer after low anterior resection
2	rejection of NAPNA
1	APER against expectation

Reasons overlapped. Forty-eight of 53 patients were not informed of NAPN before surgery. *APER*, Abdomono-perineal excision of the rectum; *NAPNA*, neo-anus with a pudendal nerve anastomosis.

Surgical procedure (Fig 1). An abdominal approach for APER was performed in the conventional manner in our hospital. After the left colon was mobilized and transected in the sigmoid colon, we constructed a colonic S-pouch (35 mm in size with a conduit 35 mm in length)[19] in 12 patients and a coloplasty-pouch[20] in 5 patients, but did not construct any pouch in the other 2 patients. We did not construct a J-pouch because the pouch must be located above (outside) the new anal canal.

A NAPNA was reconstructed by using a right-sided gluteus maximum muscle[21] (GMM) and a right-sided pudendal nerve contemporaneously with anorectal resection in a prone position after the abdominal procedure in all patients (Fig 1, *A*). Two types of skin incision were used: a long inverted U-curved incision in 3 early patients[18,19] and a modification involving a division of the incision into 2 smaller incisions in the last 16 patients in an attempt to decrease the risk of skin necrosis.

After the inferior portion of GMM (iGMM) was everted to the perineum (Fig 1, *B*), only the branches innervating the iGMM of the inferior gluteal nerve (IGN) were transected and microsurgically anastomosed with the central end of the transected pudendal nerve (Fig 1, *C* and *D*).The iGMM was wrapped around the sigmoid colon (Fig 1, *E*) to act as a sphincter and then brought down through the pelvis and connected to the perineum.

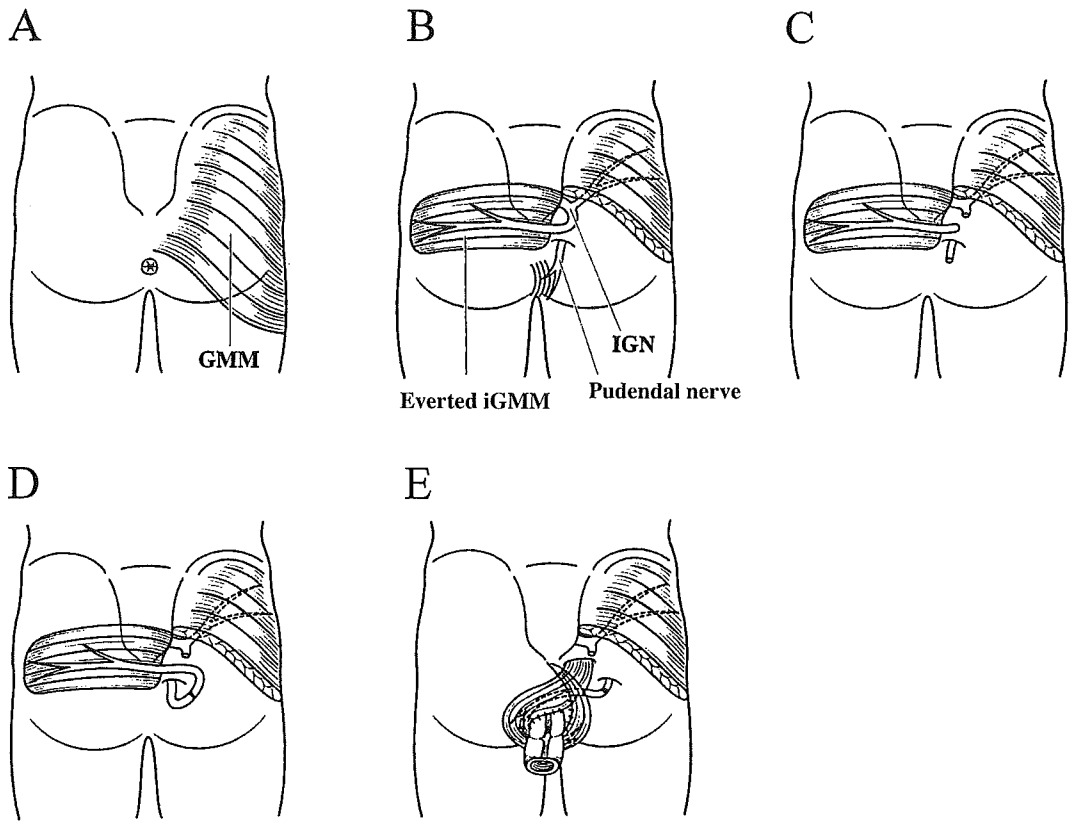

Fig 1. A, A neo-anus was reconstructed in a prone position just after an abdominal approach of APER. After the iGMM was everted to identify the IGN (**B**), the branch of the IGN innervating the iGMM was transected at the origin with preservation of the original innervation of the IGN to the upper part of GMM (**C**). The distal cut end of the IGN innervating the iGMM was microsurgically anastomosed to the central end of the transected pudendal nerve by using the technique of the epineural anastomosis (**D**). The iGMM after the pudendal nerve anastomosis was transposed to the perineal wound and was wrapped around the sigmoid colon (a conduit of the colonic S pouch) (**E**), which was brought down through the pelvis and connected to the perineum.

A diverting ileostomy was constructed on the abdomen with plans to take it down after the reinnervation of the pudendal nerve or at the beginning of the neo-sphincter contraction.

Evaluation. We evaluated the NAPNAs based on the clinical outcomes, the anorectal manometry, the defecatory status, the QOL, and the occupation status after surgery. All complications and events were recorded at the time of their occurrence. In anorectal manometry, the pressure and length of the neo-anal canal were measured with the use of a circular microtransducer 4 mm in diameter and 5 mm in length.[22] Maximum tolerant volume and minimum volume to sense the need to defecate were measured with the use of an intra-neorectum balloon.

The defecatory status was assessed with the use of a questionnaire based on the Cleveland Clinic Florida incontinence scoring system,[23] in which the scoring of fecal incontinence is based on the frequency of incontinence of formed stool, fluid stool, and gas, respectively, as well as the frequency of using pads and the frequency of lifestyle disruption in the previous 4 weeks. The frequencies of 0/4 weeks, 1/4 weeks, 2-3/4 weeks, more than once a week but not every day, and every day were allotted the following scores, respectively: 0 point, 1 points, 2 points, 3 points, and 4 points. Full continence is designated by 0 points; complete incontinence is designated by 20 points. Patients were also asked about the frequency of defecation, the duration of using the toilet, and the predominance of fecal incontinence between sleeping and daytime activities.

The QOL was assessed with the use of a questionnaire based on the WHOQOL-BREF, which is an international scoring system of QOL established for comparisons between different countries by the World Health Organization.[24] QOL was scored in 5 categories independently: physical, psycho-

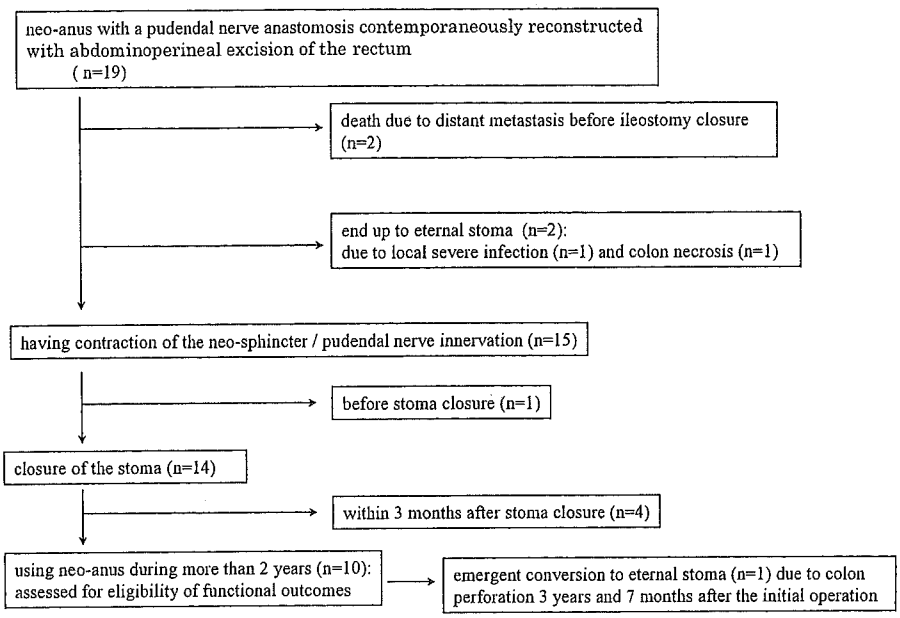

Fig 2. Clinical course. Data were tallied on January 1, 2003.

logic, social, environmental, and general QOL; then the average of these QOLs was calculated. Five points represents the best QOL and 1 point represents the worst.

The satisfaction regarding the NAPNA was compared to each patient's satisfaction with his or her ileostomy (ie, intrapatients comparison). In addition, the QOL was compared between the patients with NAPNA and the patients with conventional APERs (ie, interpatient comparison).

Statistical analysis was performed with the Mann-Whitney *U* test and the Fisher exact test. The surgeries were approved by the medical ethical committee of Jichi Medical School Hospital.

RESULTS

Clinical course (Fig 2). No surgical mortalities were seen. Early distant metastasis (but without local recurrence) resulted in 2 patients being dropped from the functional study of the neo-anus; their diverting ileostomies were not finally taken down. Another 2 patients ended up with permanent colostomies without any use of NAPNAs because of partial removal of the neo-sphincter that was induced by the perineal wound infection[18] and ischemic necrosis of the terminal colon, which was pulled down to the perineum. A recent patient was waiting for the closure of his or her ileostomy after innervation of the pudendal nerve.

The neo-sphincter began contracting on average (n = 15) at 6.6 ± 1.8 months after the pudendal nerve anastomosis, then the ileostomy was taken down on average (n = 14) at 9.1 ± 2.6 months after surgery. While 4 of the 14 patients were within 3 months after the ileostomy closure, we studied the long-term outcomes (ie, for more than 2 years) of function, defecatory status, and the QOLs in another 10 patients. In terms of clinical course, all of the 10 had colonic S-pouches. The median period of using a NAPNA after closure of the covering stoma was 36 months (range, 26-68 months) in the 10 patients. In 1 patient, at 3 years and 7 months after the initial surgery, a permanent colostomy was emergently constructed due to perforation of the colonic S pouch a week after colonoscopic examination for postoperative surveillance.

In the early 3 patients using a long skin incision, major skin necrosis (ie, with a skin defect remaining more than 1 month) occurred. In 1 patient, the final outcome was permanent colostomy.[18] In another patient, the rewrapping operation of the neo-sphincter was also performed due to the dehiscence of anchoring neo-sphincter.[19] The reduction in the degree of skin incision (by using 2 small incisions) decreased skin problems to major skin necrosis in 3 patients and minor skin necrosis in 5 of the 16 patients. Obstruction of the small intestine led to necessary surgery in 2 patients. Anal narrowing led to anal dilatation using a dilator in 2 patients.

Table II. Incontinence score, quality of life and satisfaction in patients with neo-anus

Case No.	*Age*	*Sex*	*Incontinence for*			*Usage of pads*	*Lifestyle*	*CCFIS*	*Average of WHOQOL-BREF*
			Formed stool	*Diarrhea*	*Gas*				
Younger group									
2	54	M	2	0	4	4	0	10	3.69
3	57	M	1	2	0	3	0	6	3.81
6	46	M	3	2	2	4	1	12	3.35
9	49	M	2	2	1	4	1	10	3.25
12	47	M	2	1	1	4	3	11	3.48
Mean	50.6		2	1.4	1.6	3.8	1	9.8	3.52
SD	4.7		0.7	0.9	1.5	0.4	1.2	2.3	0.23
Elder group									
4	67	M	2	2	3	4	0	11	3.04
5	62	M	4	0	4	4	4	16	3.54
8	67	M	3	3	3	4	3	16	3.88
10	68	M	3	3	4	4	2	16	3.73
11	70	M	4	0	3	4	3	14	3.5
Mean	66.8		3.2	1.6	3.4	4	2.4	14.6	3.54
SD	2.9		0.8	1.5	0.5	0	1.5	2.2	0.32
Overall									
Mean	58.7		2.6	1.5	2.5	3.9	1.7	12.2	3.53
SD	9.3		0.97	1.18	1.43	0.32	1.49	3.29	0.26
P value	0.009		0.049	0.661	0.068	0.317	0.163	0.019	0.602

CCFIS, Cleveland Clinic Florida incontinence score; *SD*, standard deviation; *NA*, not available.

Defecation status (Table II). All patients defecated without irrigation. Binding medicine was used in 4 patients (40%); laxatives were used in 3 patients (30%). The frequency of defecation was 4.8 ± 2.6 times/day, and the duration was 14.6 ± 9.9 minutes/toilet. Thus, 62.2 ± 48.9 minutes were spent on the toilet each day by count. The Cleveland Clinic Florida fecal incontinence score was 12.2 ± 3.3 points overall. The fecal incontinence predominantly occurred during the patients' sleep in 5 of 9 (55.6%) patients who answered. No patients wished to go back to their lives with a stoma. Four patients (40%) reported being capable of distinguishing gas from stool. Eight (80%) patients clearly stated that their condition with the NAPNA was better than with the ileostomy. The other 2 (20%) patients answered that life with NAPNA was equal to that with an ileostomy and reported they had daily fecal incontinence for formed stool.

Seven (70%) patients answered that they would recommend the NAPNA procedure to friends or family who suffered from rectal cancer; the other 3 (30%) answered that they would hesitate to make such a recommendation. No patients (0%) answered that they would advise their friends or family against undergoing NAPNA.

Quality of Life (Fig 3). The average of WHOQOL-BREF in patients with NAPNAs was significantly better than that in patients with a stoma after conventional APERs ($P = .0402$).

Relationship between age and outcomes (Table II). Of the 5 patients under 60 years old, 4 (80%) discriminated between gas and stool, while none of 5 patients over 60 discriminated between gas and stool ($P = .0476$). There was also a significant difference in the Cleveland Clinic incontinence score ($P = .0192$) and the frequency of formed stool ($P = .0486$) between these 2 groups. In addition, there was a significant difference in Cleveland Clinic incontinence score ($P = .0299$) and the frequency of lifestyle disruption ($P = .0485$) between patients with and without sensitivity. However, no significant difference was seen in WHOQOL-BREF.

Manometry. There was no significant difference between the group of patients younger and the group of patients older than 60 years (Table III).

Hospital stay. The median hospital stay after NAPNA surgery was 35.5 days (SD, 52.2 days) in 19 patients, with the first 3 patients with large skin incisions staying 65 days and the 16 patients using the modified skin incisions staying 35 days. The median hospital stay in 53 patients after a conven-

Physical QOL	*Psychologic QOL*	*Social QOL*	*Environmental QOL*	*General QOL*	*Discrimination between gas and stool*	*Recommendation*	*Comparison with ileostomy*
4	3.67	3	3.75	3.5	Yes	Yes	Better
4.29	4.17	3.33	3.25	3.5	Yes	Yes	Better
3.57	3	3	3.63	3	Yes	Yes	Better
3.83	3	3.33	3.13	25	Yes	Yes	Better
3.43	3.6	3.33	3.63	3	No	Yes	Better
3.82	3.5	3.2	3.48	3.1			
0.34	0.5	0.18	0.27	0.42			
3.29	3.17	2.67	2.88	3	No	Suspension	Better
3.57	3	3.33	4.37	2	No	Suspension	NA
3.71	4.17	3.5	3.88	4	No	Yes	Better
4.29	3.5	3.67	3.63	3	No	Yes	Better
3.43	3.5	3	3.88	3	No	Suspension	NA
3.66	3.47	3.23	3.73	3			
0.39	0.45	0.4	0.55	0.71			
3.74	3.48	3.22	3.6	3.05			
0.35	0.45	0.29	0.43	0.43	0.55		
0.399	0.832	0.662	0.243	0.737	0.048	0.167	0.444

tional APER was 33 days (SD, 21.1 days). No significant difference was seen in the hospital stay between APER and NAPNA in the recent 16 patients ($P = .2523$)

Occupation. Two of 10 patients had already been retired before surgery. The remaining 8 patients (100%) worked in some capacity after surgery. Four (50%) of the 8 patients kept the same occupation before and after surgery. Another patient (13%) temporarily lost his occupation because of suffering from rectal carcinoma but started a new venture business after undergoing a NAPNA. Three (38%) changed their jobs after surgery.

DISCUSSION

The aim of the pudendal nerve anastomosis was recovery of the proper functions of the original anal sphincter, which were innervated by the pudendal nerve.[16] According to the evidence of conversion of both the muscle fiber type and the electromyographic pattern of the neo-sphincter from the GMM to the original anal sphincter in the human patients[18, 19] and in animal studies,[16,25] the neo-anal sphincter was regenerated on a base of GMM. A NAPNA should be categorized as tissue engineering (regeneration) rather than reconstruction of the anus.

Despite the imperfect continence associated with a NAPNA, no patients wished to return to life with a stoma, and no patients lost their occupation. The satisfaction of life with a NAPNA was superior to that with an ileostomy in 80% of the patients; furthermore, the QOL with a NAPNA was significantly better than that with a stoma after a conventional APER. These findings indicated that NAPNA could be an option that benefits patients after an APER.

Because all of the systems for controlling defecation are removed in an APER, a neo-anus should ideally cover all of the functions of the anus and rectum (ie, sphincteric power, coordinated movement with the defecation, receptor mechanism to sense the need to defecate, and reservoir function). Which factor is the most important with a neo-anus? The key factor was considered to be the sensory function involved with the recognition of the need to defecate. Forty percent of the patients with a NAPNA were capable of knowing they needed to defecate and 80% of them were capable of discriminating between gas and formed stool; such patients possessed significantly better Cleveland Clinic Florida incontinence scores and expressed a high degree of satisfaction. However, there was no significant relationship between the anal pressures and the incontinence scoring or the satisfaction.

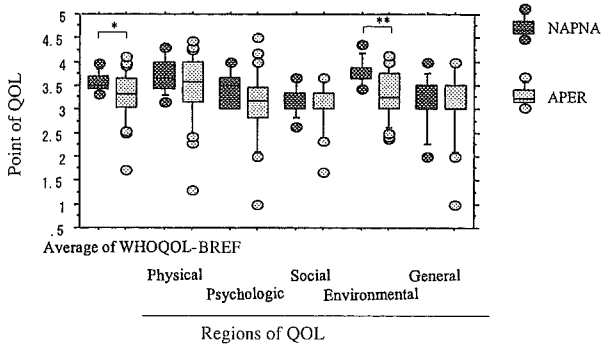

Fig 3. Quality of life (WHOQOL-BREF) in patients with a NAPNA and in patients after an APER. *$P = .04$; **$P = .002$. *NAPNA,* Neo-anus with a pudendal nerve anastomosis; *APER,* abdomino-perineal excision of the rectum.

The recovery rate (40%) of the sensitivity in this series was considered quite high because it was reported previously to be very difficult for the sensitivity to return in patients with a neo-anus along with an electrically stimulated neo-sphincter.[26] The recovery of the sensitivity after a NAPNA may be followed by the reflexive contraction of the neo-sphincter as was proved after the reinnervation of the pudendal nerve in our previous animal study.[16] It was advantageous that patients with sensitivity could go to the lavatory at a reasonable time. That was why patients with sensitivity had higher satisfaction and better incontinence scores ($P = .0299$), corresponding to previous reports that stated that the sensitivity played an important role in obtaining an acceptable degree of continence with an electrically stimulated neo-sphincter.[8,12,26] In addition, it was also advantageous that irrigation was not conducted in any patients with a NAPNA, although irrigation was commonly conducted in patients with electrically stimulated neo-sphincter.[4,5,6,26] This difference possibly results from the fact that high anal pressure was not required for patient satisfaction after the procedure of a NAPNA. We stress that the clinical success in NAPNAs was attributable to recovery of the sensitivity or the innervation of the pudendal nerve in the neo-sphincter. However, patients with this sensitivity also stated that they did not experience a sensation to excrete small stools, which confounded them. It may be difficult to achieve this complete level of sensitivity.

Since all 4 patients who were capable of recognizing the need to defecate were under 60 years old and they had significantly better fecal incontinence scores, patients under 60 years old may be well indicated for a NAPNA, although all patients older than 60 years old would not be contraindicated.

Table III. Manometric data

Case No.	*SP*	*RP*	*LAC*	*MinV*	*MaxV*
Younger group					
2	136.3	43	60	20	150
3	82.8	25.4	60	30	150
6	250.9	21.3	46	NA	NA
9	239.4	27.7	31.3	30	NA
12	103.3	37.6	39	90	130
Mean	162.6	31	47.3	42.5	143.3
SD	77.9	9	12.7	32	11.5
Elder group					
4	180	23	46	45	120
5	134.6	35.5	32	70	160
8	113.3	19.3	44.4	20	220
10	57.6	17.8	33	30	110
11	52.5	42.6	32	NA	NA
Mean	107.6	27.64	37.48	41.25	152.5
SD	53.7	10.9	7.1	21.7	49.9
Overall					
Mean	135.1	29.3	42.4	41.9	148.6
SD	69.4	9.6	11	25.3	36.3
P value	0.251	0.348	0.292	0.882	>0.999

SP, Squeezing pressure; *RP,* resting pressure; *LAC,* length of anal canal; *MinV,* minimum volume to sense to defecate; *MaxV,* maximum tolerant volume; *NA,* not available.

The perineal infection followed the skin necrosis and caused the prolonged hospital stay. The perineal wound, however, could finally withstand the infection in all patients except for a patient with colon necrosis. This observation may be because the massive neo-sphincter muscle was transplanted to the perineum to fill the dead space without any foreign body. The feasible salvageablity of a NAPNA from the infection was a great advantage, while the local infection was reported to be refractory in other neo-anus surgeries using foreign bodies (an artificial neo-sphincter and an electric stimulator).[11,27]

CONCLUSION

The NAPNA patients had significantly better QOL scoring compared to patients who had undergone conventional APERs; the NAPNA satisfied 80% of the patients. Despite incomplete continence with a NAPNA, no patients lost their occupation or wanted to go back to life with a stoma. The sensitivity to recognize the need to defecate was a key to good patient satisfaction. Although the NAPNA surgery still needs further modifications in terms of operative detail, now it can be considered a practical option for selected patients wishing to avoid a stoma after an APER.

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ORIGINAL ARTICLE

Distribution of lymph node metastasis in T1 sigmoid colon carcinoma: Should we ligate the inferior mesenteric artery?

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Abstract

Objective. In standard oncological sigmoid colectomy, the inferior mesenteric artery is ligated either at its origin or at the level of the left colic artery. However, in patients with early-stage carcinoma, the distribution of metastatic nodes may be limited. The aim of this study was to clarify the prevalence and distribution of lymph node metastasis in T1 sigmoid colon carcinoma and to determine the adequate range of lymph node dissection. ***Material and methods***. The study included 121 consecutive patients treated for T1 sigmoid colon carcinoma. Clinicopathologic factors associated with nodal metastasis and the distribution of metastatic nodes were analyzed. ***Results***. Of 121 patients, 12 (10%) had nodal involvement. The depth of invasion and the presence of lymphatic and vascular invasion were significantly associated with nodal metastasis. Of these 12 patients, 11 (92%) had lymph node metastasis confined to pericolic nodes. Nodes along the sigmoidal artery were involved in one patient. There was no involved node along the superior rectal artery or at the root of the inferior mesenteric artery. ***Conclusions***. Lymph node dissection for T1 sigmoid colon carcinoma should be limited to the root of the sigmoidal artery, and the inferior mesenteric artery should be preserved.

Key Words: *Lymph node metastasis, lymph node dissection, T1 colon cancer*

Introduction

There are two treatment options for T1 colon cancer: surgical resection (SR) and endoscopic resection (ER). SR and ER are indicated for lesions with and without risk of lymph node metastasis, respectively. The risk of lymph node metastasis is determined from the pathological findings, such as the depth of invasion into the submucosal layer, lymphatic or vascular invasion, and tumor differentiation [1–5]. The indication for ER is evaluated by conventional and magnification chromocolonoscopy, by which the depth of the tumor can be predicted with more than 80% accuracy [6,7]. If submucosal invasion is considered to be minimal, ER is attempted and the risk of nodal metastasis is evaluated by pathological examination of the resected specimen.

Oncological colectomy consists of resection of the affected bowel and nodal dissection with an adequate margin. Generally, nodal dissection up to the root of the corresponding artery is the standard procedure. However, the distribution of metastatic nodes may be limited in patients with T1 colorectal cancer, and less aggressive nodal dissection than that with the standard procedure can be performed in such patients, without increasing the risk of recurrence. The aim of this study was to clarify the prevalence and distribution of lymph node metastasis in T1 sigmoid colon cancer, in order to determine the adequate extent of nodal dissection.

Material and methods

From 1979 to 2001, 356 patients with T1 colorectal cancer were treated at Jichi Medical School. Of these, 121 consecutive patients with T1 sigmoid colon cancer were included in this study.

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Our treatment policy was as follows: 1) Depth of invasion of the tumor was assessed by means of both conventional and magnification chromocolonoscopy with the aid of a dye spray technique. Endoscopic ultrasonography was performed if considered necessary. 2) If the depth of submucosal invasion was estimated to be minimal, ER was attempted. If the depth of submucosal invasion was estimated to be massive, SR was performed as primary treatment. When it was not possible to estimate the depth of submucosal invasion and ER was considered technically feasible, ER was attempted. 3) If pathological examination of the endoscopically resected specimen revealed "unfavorable" features such as a positive resection margin, massive invasion adjacent to the vertical resection margin, submucosal invasion of more than 1000 μm, lymphatic or vascular invasion, or poor differentiation, SR was performed.

The clinicopathological characteristics of the patients and the distribution of lymph node metastasis were analyzed. Lymph nodes were classified according to their location: pericolic nodes (PCN), nodes distributed along the sigmoidal artery (SAN) and superior rectal artery (SRN), and nodes at the root of the inferior mesenteric artery (IMN). The depth of invasion into the submucosal layer was measured by microscopy.

All patients were enrolled in our follow-up program, which consists of multidetector-row abdominal CT and plain chest X-ray every 3 months for the first 2 years and every 6 months for the next 3 years, and determination of serum level of CEA every 3 months for 5 years. Swelling of lymph nodes along the aorta and around the root of the mesenteric artery was carefully monitored, mainly by CT. All patients were followed for at least 30 months after resection.

For statistical analysis, Fisher's exact test and Student's t-test were used, and a p-value of less than 0.05 was considered significant.

Results

Patient characteristics are presented in Table I. The study subjects comprised 88 men and 33 women, mean age 61.9±9.4, range 36–90 years. SR was performed as primary treatment in 46 patients. ER was performed as primary treatment in 75 patients, 60 of whom underwent further SR because of unfavorable feature(s). Nodal metastasis was present in 12 patients (10%).

In Table II, clinicopathological factors are compared between patients with and without nodal metastasis. Depth of invasion, lymphatic invasion and vascular invasion were significantly correlated with nodal metastasis.

Table I. Patients' characteristics.

Gender (Male/Female)	88/33
Age (±SD)	61.9±9.4
Treatment*	
SR	46
ER	15
ER+SR	60
Differentiation	
Well	108
Moderate	12
Sig.	1
Nodal metastasis	
None	109
Pericolic	11
Intermediate**	1

Abbreviations: SR = surgical resection; ER = endoscopic resection.
**Node along the sigmoidal artery.

The clinicopathological features of the 12 patients with nodal metastasis are presented in Table III. All but one underwent SR. In the patient who did not undergo SR, lymph node metastasis was detected during the follow-up. In the other 14 patients who underwent ER as the only treatment, follow-up examinations did not reveal nodal metastasis. Of the 12 patients with nodal metastasis, 11 (92%) had lymph node metastasis confined to PCN. A SAN node was involved in one patient. There was no nodal involvement of SRN or IMN in our series.

Table II. Nodal metastasis and clinicopathological factors.

	Node negative	Node positive	p-value
Age	61.4±9.4	66.3±8.2	0.08
Size (mm)	19.5±9.8	20.1±13.1	0.73
Differentiation			
Well	99	9	0.32
Moderate	9	3	
Sig.	1	0	
Depth of invasion* (mm)	2.6±2.8	4.3±1.1	0.05
Lymphatic invasion**			
−	93	5	<0.001
+	9	6	
++	2	0	
+++	0	1	
Vascular invasion***			
−	99	8	0.0003
+	5	3	
++	0	0	
+++	0	1	

*Depth of invasion was not assessed in three cases. **Lymphatic invasion was not assessed in five cases. ***Vascular invasion was not assessed in five cases.

Table III. Cliniocopathological factors of patients with nodal metastasis.

Gender	Age	Treatment	Size (mm)	Differentiation	Depth of invasion (mm)	ly	v	Location of positive node(s)
M	60	SR	12	Well	2.5	+	−	Pericolic
F	79	SR	25	Well	3.2	+	+	Pericolic
M	79	SR	56	Well	3.8	+	−	Pericolic
M	52	SR	18	Moderate	3.9	+	+++	Pericolic
M	65	SR	32	Moderate	3.9	+++	+	Pericolic
M	65	ER-SR	11	Well	4.8	−	−	Pericolic
M	60	ER-SR	15	Well	4.9	−	−	Pericolic
M	65	ER-SR	8	Well	4.9	+	−	Pericolic
F	72	ER-SR	22	Well	5.8	−	−	Pericolic
M	73	ER-SR	18	Well	ND	−	−	Pericolic
F	59	ER	10	Moderate	ND	+	+	Pericolic
M	67	ER-SR	20	Well	6.0	−	−	Intermediate

Abbreviations: SR = surgical resection; ER = enscopoic resection; ER-SR = endoscopic resection followed by surgical resection, ly = lymphatic channel invasion, v = vascular invasion.

Discussion

Oncological colectomy consists of resection of the bowel and lymph node dissection with an adequate margin. The standard procedure for lymph node dissection is wide resection of the mesentery with high [8–14] or low [15–23] ligation of the corresponding artery. For sigmoid colon cancer, that means ligation of the inferior mesenteric artery. After ligation of the inferior mesenteric artery with either a high or low tie, blood to the remaining intestine distal to the resection margin is supplied from the internal iliac artery. In certain cases of sigmoid colon cancer, the colon is resected more distally than determined solely by oncological features, because of the risk of ischemia resulting from ligation of the inferior mesenteric artery.

Of these 11 patients with nodal metastasis, the location of the positive nodes was PCN in 10 patients and in the other patient the involved node was located along the sigmoidal artery. There was no lymph node metastasis along the inferior mesenteric artery and superior rectal artery in 121 patients with T1 sigmoid colon carcinoma. Therefore, ligation of the inferior mesenteric artery or superior rectal artery was considered to be unnecessary.

Previous reports have claimed that the number of harvested lymph nodes correlates significantly with the long-term results in patients with colon carcinoma, and advocated the importance of pathological examination of 12 to 15 or more nodes [24–32]. Limited lymph node dissection with preservation of the inferior mesenteric artery may result in a decreased number of harvested nodes. However, increasing the number of nodes by dissection of distant cancer-free nodes is considered to have no clinical impact [33].

Ligation of the inferior mesenteric artery may be associated with complications. A randomized controlled trial by Tocchi et al. demonstrated that the prevalence of anastomotic leakage was higher with ligation than with preservation of the inferior mesenteric artery [34]. Autonomic nerve injury is another possible complication of high ligation [35,36].

Preoperative assessment of the depth of invasion is essential in making the decision on whether to perform limited nodal dissection. We consider that tumor extirpation by means of endoscopic resection is the most reliable method to obtain a definitive diagnosis concerning the depth of invasion as well as other pathological factors associated with nodal involvement. In our series of 121 patients with T1 sigmoid colon cancer, 75 underwent ER as the first treatment and 60 subsequently underwent SR because of unfavorable pathological findings. These 60 patients (50%) were thought to be candidates for limited nodal dissection. These figures might be increased by progress in endoscopic instruments and technique.

We conclude that lymph node dissection for T1 sigmoid colon carcinoma can be limited to the roots of the sigmoidal artery, and the inferior mesenteric artery and superior rectal artery can be preserved without jeopardizing the surgical curability. A limited dissection policy may benefit patients with T1 sigmoid colon cancer by subjecting them to less invasive surgery.

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Rectovaginal fistulas after rectal cancer surgery: Incidence and operative repair by gluteal-fold flap repair

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Background. *We investigated the correlation between operative procedures for rectal carcinoma and postoperative rectovaginal fistulas (RVF), and treatment for RVF.*
Methods. *The medical records of 161 female patients with rectal carcinoma were examined retrospectively with respect to the cause, incidence, and methods of treatment for RVF occurring after rectal cancer operations, and to the outcomes of gluteal-fold flap repairs for RVF.*
Results. *Of the 161 patients, 16 developed RVF clinically. The incidence of RVF was significantly higher in patients who were anastomosed by the double stapling technique (DST) and had concomitant resection of the vaginal wall. No statistical difference was found between the established diverting ostomy group and the no-stoma group. Six patients recovered by the establishment of a diverting ostomy only. The gluteal-fold flap technique was performed for 5 patients. No RVF recurrences were noted in these 5 patients.*
Conclusions. *The incidence of RVF was higher in the patients who were anastomosed by DST or had concomitant resection of the vaginal wall. Although some RVFs heal with only fecal diversion, for patients in whom RVF is caused by involvement of the vaginal wall in the circular staple or intersphincteric resection, good results are obtained with the gluteal-fold flap repair technique.*
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FOR PATIENTS WITH LOW RECTAL CARCINOMA, a coloanal anastomosis or low colorectal anastomosis using double stapling has become popular.[1-4] This anastomotic method may sometimes result in rectovaginal fistula (RVF) as a clinical technical complication although most surgeons are alert to this complication.[5-6] Furthermore, anastomotic leakage often causes RVF when an intrapelvic abscess penetrates the posterior vaginal wall.

Crohn's disease, cryptoglandular disease, and obstetrical injury are known causes of RVF. Various methods of repair of RVF arising in these diseases and as a complication of rectal cancer surgery have been used, including the use of a mucosal advancement flap,[7-9] a transsphincteric approach that combines a rectal mucosal advancement flap and an anal sphincteroplasty,[10] fibrin sealant instillation,[11] an ileal pouch mucosal advancement flap or circumferential pouch advancement, and a protectomy with colonic pull-through and delayed coloanal anastmosis.[5,8] Of these methods, an endoanal and endovaginal advancement flap is the most frequently used technique. However, RVF repairs sometimes break down when patients undergo RVF repairs more than once.[12] In 1996, the lotus petal flaps procedure was reportedly used to reconstruct a vulvovaginal defect.[13] We adapted this flap method—the gluteal fold flap—for treatment of RVF in postoperative patients with rectal cancer who have undergone intersphincteric resection or for patients in whom RVF resulted from involvement of the posterior wall of the vagina in a circular stapled anastomosis. Few studies have examined the clinical features, operative methods,

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anastomotic technique, and establishment of a diverting ostomy for postoperative RVF. We retrospectively investigated the relationship between operative procedures and RVF, and whether a gluteal-fold flap repair is an effective and simple solution for the treatment of RVF.

PATIENTS AND METHODS

The medical records of 204 patients undergoing treatment for primary rectal cancer during July 1992 to November 2002 at our institute were reviewed. Forty-three patients who underwent abdominoperineal resection, Hartmann's operation, or total pelvic exenteration were excluded. The remaining 161 patients who underwent sphincter-preserving surgery were retrospectively examined. Of these 161 patients, high anterior resection (HAR) was performed for 34 patients, low anterior resection (LAR) for 81 patients, very low anterior resection (vLAR) for 39 patients, and intersphincteric resection (ISR) for 7 patients.

Of the 161 patients, 8 patients had diabetes and 12 had vascular disease (eg, angina pectoris and arteriosclerosis). No patients had inflammatory bowel disease. Only 4 of the 161 patients who underwent an ISR received preoperative radiotherapy. The total dose of radiation delivered through a linear accelerator was 45 Gy in 25 fractions over 5 weeks, followed by an operation 2 weeks later. The vaginal wall was opened intraoperatively in 26 patients (16.1%), either because of concomitant hysterectomy with closure of the vaginal stump (n = 5) or as part of the resection of the posterior vaginal wall due to cancerous invasion (n = 21).

A straight coloanal or colorectal anastomosis was accomplished by using the stapling technique or hand sewing in all 161 patients. All patients underwent anastomosis by the single stapling technique (SST) (n = 84; 52.2%), double stapling technique (DST) with a circular stapler (n = 65; 40.4%), or coloanal anastomosis with hand sewing (n = 12; 7.4%). At the time of the anastomosis with the circular stapler, the completeness of all stapler donuts was confirmed by the surgeons. If a stapler donut was incomplete, we tested the anastomotic site for patency with air and sewed up the leakage point of the anastomosis to provide reinforcement with absorbable interrupted sutures. A diverting loop ostomy was established in 79 patients (49.1%) at the initial operation. One or two drains (Pleats Drainage Tube MD-45110, external diameter 10 mm; Sumitomo Bakelite, Tokyo, Japan) were introduced to the posterior and/or anterior side of the colorectal anastomosis. None of the patients had omental interposition of preventive measures for RVF.

Diagnostic evaluation of the patients with RVF included gastrografin enema and/or digital examination after postoperative vaginal flatus, fecal leakage, and/or vaginal discharge were clinically presented.

The cause and incidence of RVF in every operative procedure were examined. Statistical analysis was performed with the chi-square test for independence for comparison between operative methods and the incidence of RVF. A probability value of $P < .05$ was designated as statistically significant for all analysis.

The results of some surgical treatments for RVF and outcomes of the patients who underwent gluteal-fold flap repair were analyzed. Written informed consent was obtained from all patients before the gluteal-fold flap repair. An ethics committee approved the operative treatment for RVF in the rectal cancer patients.

Gluteal-fold flap repair technique for RVF. The patient undergoes a mechanical bowel preparation preoperatively; then, under general anesthesia, the patient is placed in the lithotomy position and the RVF identified. A solution of 1:500,000 adrenalin in saline is injected under the posterior vaginal mucosa, and a transvaginal incision is then made around the RVF. The edges of the incision are undermined circumferentially just over the external rectal muscular layer. The fistula is probed and debrided. The rectal opening of the fistula is then closed with the use of 2 layers of absorbable sutures in an interrupted horizontal mattress fashion (Fig 1).

To adequately cover the closed rectal fistula, we designed the gluteal-fold, which is a triangular or diamond-shaped flap consisting of skin, subcutaneous fat, and superficial fascia (Fig 2). A skin incision is made at the posterolateral margin of the vaginal introitus with some perforators of the internal pudendal artery being used as a pedicle for the flap. We did not mark the points of the perforators of the internal pudendal artery with a Doppler probe. We constructed some perforators of the internal pudendal artery in the fatty tissue to act as a pedicle or an axis of the flap; then, we used thinned subcutaneous fatty tissue to adjust the vaginal mucosal thickness. The flap is turned 180 degrees and then advanced into the vagina (Fig 3), where it is sutured to the vaginal mucosal defect above the fistula and closed with the use of absorbable interrupted sutures. The gluteal skin defect is closed directly (Fig 4). Drains are introduced

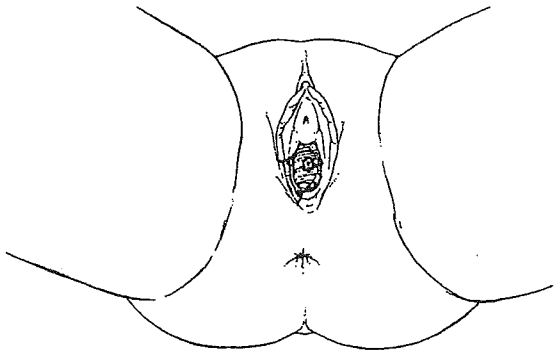

Fig 1. A transvaginal incision, with the edge being undermined circumferentially just over the external rectal muscular layer, is made around the RVF; the rectal opening of the fistula is then closed with the use of 2 layers of absorbable suture in an interrupted horizontal mattress fashion.

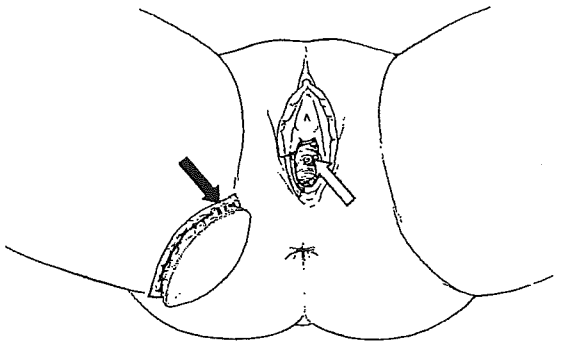

Fig 2. A diamond flap consisting of skin, subcutaneous fat, and the superficial fascia is designed in the glutealfold. Some perforators of the internal pudendal artery in the fatty tissue are constructed to act as a pedicle or an axis of the flap (*black arrow*). The *white arrow* indicates the position of the RVF.

under the subcutaneous tissue of the skin flap. A diverting loop ostomy is established at the ileum or transverse colon if this procedure has not already been performed.

Prophylactic antibiotic coverage is used for 3 days. The drain is removed 5 to 7 days after surgery, and the patients are permitted to walk and sit 7 days after surgery. The diverting loop ostomy is closed 3 to 6 months later to ensure the RVF has healed without recurrence, as determined by barium enema examination.

RESULTS

Table I shows the correlation of the incidence of RVF with the operative method. Of the 161 patients, RVF occurred clinically in 16 (9.9%). The onset of postoperative RVF ranged from 3 to

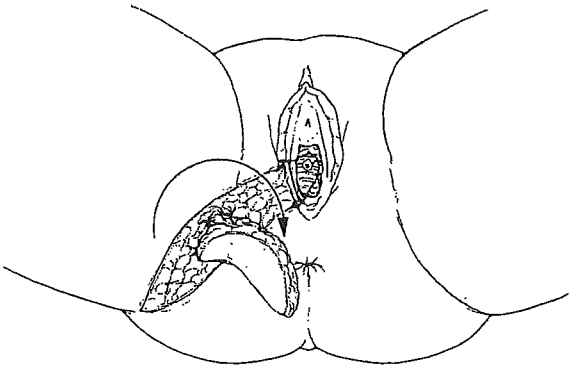

Fig 3. Flap is turned 180 degrees and then advanced into the vagina.

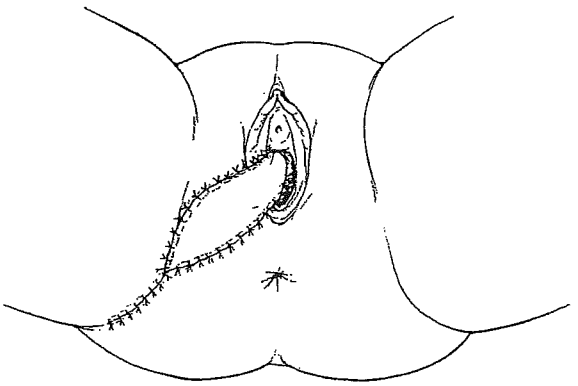

Fig 4. Flap is sutured to the vaginal mucosal defect above the fistula and closed with the use of absorbable interrupted sutures.

21 days after rectal cancer operations, (mean ± SD; 11.5 ± 6.2 days). Ideally, the symptoms of 16 patients with RVF were vaginal flatus and fecal leakage (n = 7), and vaginal discharge (n = 9). RVF was found in 6 of the patients who underwent LAR (7.4%), 7 of the patients who underwent vLAR (17.9%), and 3 of the patients who underwent ISR (42.8%). No statistical differences in RVF incidence were observed between LAR and vLAR ($P = .128$). However, a statistically significant difference was observed between anterior resection and ISR ($P = .0101$).

Tables II and III show the correlation between the operative procedures and the incidence of RVF. For anastomotic technique, a statistically significant difference was observed between SST and DST ($P = .00763$). In the 26 patients who underwent a concomitant hysterectomy and/or resection of the vaginal wall, 10 patients (38.5%) developed RVF. In 8 of these 10 patients, a diverting ostomy was established when the initial curative resections for rectal cancer were performed. A

Table I. The incidence of RVF according to operative procedure

	RVF(+)	*RVF(−)*
Surgical procedures		
HAR	0 (0%)	34
LAR	6 (7.4%)	75
vLAR	7 (17.9%)	32
ISR	3 (42.9%)	4
Total no. of patients	16 (9.9%)	145

RVF, Rectovaginal fistula; *HAR*, high anterior resection; *LAR*, low anterior resection; *vLAR* very low anterior resection; *ISR*, internal sphincteric resection.

Table II. The incidence of RVF for operative procedures excluding HAR

	RVF(+)	*RVF(−)*
Anastomosis technique		
SST	3 (4.8%)	59
DST	9 (15.2%)	44
Hand sewing	4 (33.3%)	8
Diverting ostomy		
(+)	9 (11.4%)	70
(−)	7 (14.9%)	41
Combined resection of uterus or posterior vaginal wall at operation for rectal cancer		
(+)	10 (38.5%)	16
(−)	6 (5.9%)	95

RVF, Rectovaginal fistula; *SST*, single stapling technique; *DST*, double stapling technique.

statistically significant difference was observed between patients with a concomitant hysterectomy and/or partial vaginectomy, and those without concomitant resection ($P < .001$). Although 5 patients who underwent a hysterectomy with closure of the vaginal stump did not develop RVF, 10 of the 21 (47.6%) patients who underwent a partial vaginectomy developed RVF. There was a statistical difference between hysterectomy and partial vaginectomy ($P = .0491$). RVF was found in 9 of the 79 (11.4%) patients in whom a diverting ostomy had already been established at the initial operation. The remaining 7 patients of the 16 patients with RVF received the diverting ostomy when RVF was confirmed. There were no statistical differences between the established diverting ostomy group and the group that did not undergo a diverting ostomy at the initial operation ($P = .545$).

The factors associated with higher rates of RVF were not seen in any preoperative co-morbid diseases (eg, diabetes and vascular disease).

Two patients did not undergo closure of the diverting ostomy due to death from metastatic tumor progression in the follow-up period. Six patients with RVF arising from anastomotic leakage recovered completely by undergoing only a diverting ostomy within 6 months postoperatively.

Table III. Details of vaginal surgery at initial operation

	RVF(+)	*RVF(−)*
Hysterectomy with closure of vaginal stump	0 (0%)	5
Partial vaginectomy	10 (47.6%)	11

RVF, Rectovaginal fistula.

Operative treatment for RVF was performed in 8 patients because a diverting loop ostomy alone did not heal the RVF. Two patients had RVF arising from partial resection of the vaginal wall in the circular stapler (1 after LAR, 1 after vLAR), and 6 had RVF arising from anastomotic leakage and abscess drainage to the vagina after a concomitant vaginal wall resection (1 after LAR, 3 after vLAR, and 2 after ISR).

The RVF healed in 1 patient who underwent re-vLAR with establishment of a diverting ileostomy. Although 1 patient underwent a transanal fistelectomy and direct closure, the RVF relapsed after closure of the diverting colostomy. A second patient underwent a diverting ileostomy; she recovered completely 2 years later. Two patients underwent repair of an endovaginal advancement flap. One patient in whom RVF arose from partial resection of the vaginal wall by double stapled anastomosis recovered after repair of the fistula with an endovaginal advancement flap 3 months postoperatively. However, in the other patient in whom the RVF arose from anastomotic leakage, the RVF relapsed despite the endovaginal advancement flap.

A gluteal-fold flap repair was performed in 5 patients who developed RVF after rectal cancer operation (Table IV): 1 from inclusion of the vaginal wall in a double stapled anastomosis, 2 from anastomotic leakage after DST in an anterior resection, and 2 from anastomotic leakage after a coloanal anastomosis with hand sewing in an ISR. The RVF was located in the higher position of the vagina in 2 patients (patients 2, 3), the middle position in 1 (patient 1), and the lower position in 2 (patients 4, 5). These 5 patients were followed for 137 to 880 days. One underwent repair of an endovaginal advancement flap; however, the RVF did not heal (patient 1).

One patient who underwent repair of an endovaginal advancement flap did not have a defunctioning ostomy constructed (patient 1), while in