

表 4 参加施設 (五十音順)

石川県立中央病院外科	四国がんセンター外科
岩手医科大学外科	自治医科大学大宮医療センター外科
大分大学消化器外科	静岡県立がんセンター外科
大阪大学消化器外科	順天堂大学浦安病院外科
大阪医科大学一般消化器外科	昭和大学横浜市北部病院消化器病センター
大阪市立総合医療センター外科	吹田市民病院外科
北里大学外科	帝京大学溝口病院外科*
北里大学東病院外科	東京医科歯科大学腫瘍外科
京都医療センター外科	東邦大学大橋病院第3外科
杏林大学第一外科	東邦大学佐倉病院内視鏡センター*
久留米大学外科	長野市民病院外科
慶應義塾大学外科	広島大学内視鏡外科
国立がんセンター中央病院大腸外科	藤田保健衛生大学外科
国立がんセンター東病院骨盤外科	横浜市立大市民総合医療センター外科
埼玉県立がんセンター外科	

(\*現在 inactive 施設)

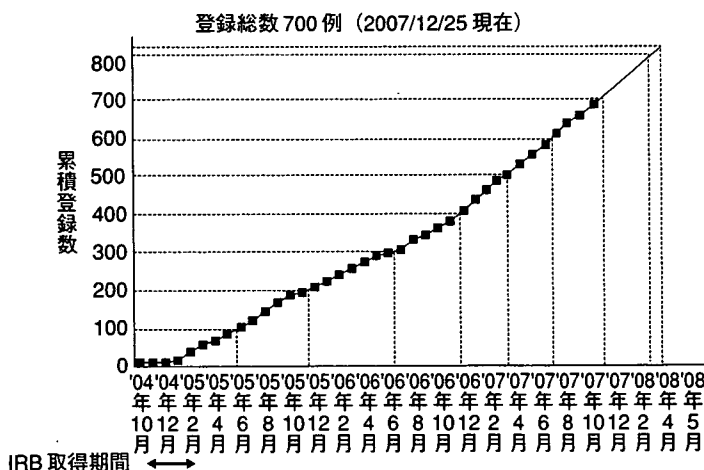


図 4 JCOG0404 累積登録状況

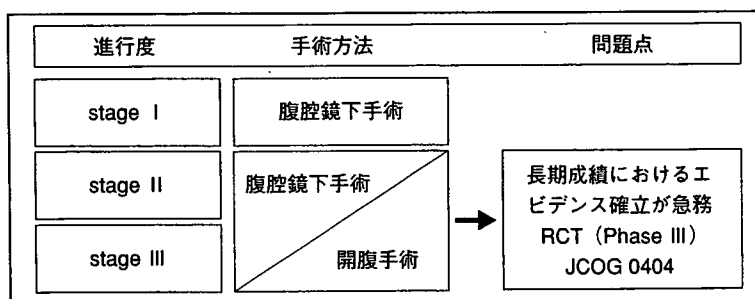


図 5 本邦における結腸癌に対する腹腔鏡下手術の位置づけ

である 5Fu/Lv 静注療法と規定, (4) 試験への参加施設および手術を施行する手術担当責任医の基準を設定, (5) 全施行症例の手術写真 (リンパ

節郭清後の術野・切除標本・創部) を研究事務局に郵送にて提出し, 年 2 回の中央判定委員会にて審査, など手術療法の RCT として quality

control と quality assurance を重視した質の高い臨床試験を目指している。参加施設は、いずれも過去の腹腔鏡下手術および開腹手術の症例数とその治療成績の審査にて承認が必要である (表 4)。2007 年 12 月現在、登録総数は 700 例という順調な進捗状況である (図 4)。本 RCT の最新情報は、Clinical trial gov<sup>13)</sup> および Umin\* にて国内外に発信されている。

### 結腸癌に対する腹腔鏡下手術の位置づけ

本稿で示した本邦の多施設共同研究と海外の RCT 結果に基づくエビデンスから、現時点における結腸癌に対する腔鏡下手術の位置づけを図 5 に示した。Stage I に対しては、腹腔鏡下手術が受け入れられており、Stage II, III に関しては根治性に関する長期成績がまだまだ十分に明らかにされていないため、本邦の大規模 RCT の結果が期待される場所である。

### おわりに

大腸癌に対する外科治療は、大きく変貌している。これは「患者にやさしい低侵襲治療」を望む社会のニーズとそれを実践させようとする腹腔鏡下手術の登場に帰するところが大きい。現時点で腹腔鏡下手術は早期結腸癌において標準治療として受け入れられているが、進行結腸癌では、エビデンスの確立や安定した手技の点から必ずしも十分とはいえない状況である。しかし、本邦で進めている進行癌を対象とした RCT (JCOG0404) の結果が明らかになれば、本邦にとどまらず世界各国の進行結腸癌に対する腹腔鏡下手術の位置づけがより明確なものになるといえよう。進行結腸癌に対する本邦で進行中の RCT の果たす意義は限りなく大きい。

\* : <http://www.umin.ac.jp/ctr/index-j.htm> : 進行大腸癌に対する腹腔鏡下手術と開腹手術の根治性に関するランダム化比較試験 (JCOG 0404, CRC Surg-LAP/OPEN)

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Current status of laparoscopic surgery for advanced colon cancer in Japan

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In Japan, a nationwide survey of JSES demonstrates that the rate of advanced colorectal cancer has increased up to 60% of total laparoscopic colorectal surgeries (LAC). A retrospective multicenter study has reported that a short and long term outcome in LAC is the same as that for open surgery. In 2003, we have just launched a prospective RCT (JCOG 0404) to compare LAC with open surgery to evaluate oncological outcome for advanced colon cancer. This trial is supported by a Grant-in-Aid for Cancer Research from Japanese Ministry of Health, Labour and Welfare. This result will be essential to clarify whether laparoscopic surgery for advanced colon cancer becomes a standard operation or not.

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## Abdominal Sacral Resection for Posterior Pelvic Recurrence of Rectal Carcinoma: Analyses of Prognostic Factors and Recurrence Patterns

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**Background:** Local recurrence of rectal cancer presents challenging problems. Although abdominal sacral resection (ASR) provides pain control, survival prolongation, and possibly cure, reported morbidity and mortality are still high, and survival is still low. Thus, appropriate patient selection and adjuvant therapy based on prognostic factors and recurrence patterns are necessary. The purpose of this study was to evaluate the results of ASR for posterior pelvic recurrence of rectal carcinoma and to analyze prognostic factors and recurrence patterns.

**Methods:** Forty-four patients underwent ASR for curative intent in 40 and palliative intent in 4 cases. All but one could be followed up completely. Multivariate analyses of factors influencing survival and positive surgical margins were conducted.

**Results:** Morbidity and mortality were 61% and 2%, respectively. Overall 5-year survival was 34%. The Cox regression model revealed a positive resection margin (hazard ratio, 10 [95% confidence interval, 3.8–28]), a local disease-free interval of <12 months (4.2 [1.8–9.8]), and pain radiating to the buttock or further (4.2 [1.6–11]) to be independently associated with poor survival. The logistic regression model showed that macroscopic multiple expanding or diffuse infiltrating growths were independently associated with a positive margin (7.5 [1.4–40]). Of the patients with recurrence, 56% had failures confined locally or to the lung.

**Conclusions:** ASR is beneficial to selected patients in terms of survival. To select patients, evaluation of the resection margin, the local disease-free interval, pain extent, and macroscopic growth pattern is important. To improve survival, adjuvant treatment should be aimed at local and lung recurrences.

**Key Words:** Therapy—Surgery—Rectal cancer—Local recurrence—Recurrence—Prognostic factor.

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Posterior pelvic recurrence<sup>1–3</sup> (PPR) of rectal carcinoma, which involves the sacrum and/or sacral nerves, presents challenging clinical problems. It may cause sacral nerve pain, perineal ulcers, fistula formation, bleeding, bowel and/or urinary tract

obstruction, sepsis, and, finally, death.<sup>4</sup> These conditions are difficult to treat, and chemotherapy provides only minimal benefits at present.<sup>4–6</sup> Radiotherapy may give pain relief, but its effectiveness is limited and temporary.<sup>4,7–9</sup> Conventional abdominoperineal resection or local excision is only palliative.<sup>10,11</sup>

In 1981, Wanebo and Marcove<sup>11</sup> reported the advantage of the abdominal sacral resection (ASR), which was first described by Brunschwig and Barber<sup>12</sup> in 1969, for PPR of rectal carcinoma. Although published data on this operation are still limited and

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there have been few long-term follow-up studies, this aggressive operation provides pain control, prolongation of survival, and possibly cure.<sup>13-22</sup> However, reported morbidity and mortality are significantly high,<sup>13-22</sup> and survival is still low.<sup>13-22</sup> Therefore, appropriate selection of patients, especially with reference to the probable prognosis, is necessary. In addition, adjuvant therapy based on recurrence patterns may be required. The purpose of this study was to evaluate the results of ASR for PPR of rectal carcinoma and to analyze prognostic factors and recurrence patterns.

### PATIENTS AND METHODS

Between March 1983 and May 2000, 44 patients with PPR of rectal carcinoma that involved the sacrum on computed tomography (CT) were considered candidates for ASR and admitted to the National Cancer Center Hospital, Tokyo. There were 35 men and 9 women, with a median age of 55 years (range, 32-73 years). Of these, 40 patients underwent initial operation at other hospitals. Selection criteria for curative-intent ASR were as follows: (1) medical fitness for ASR; (2) no signs of disseminated disease on preoperative imaging; (3) tumors involving the sacrum but not the first sacral bone and the bony lateral walls; and (4) tumors anatomically confined within the pelvis, with or without resectable solitary liver metastasis. The imaging studies routinely performed before resection were abdominal and pelvic CT, abdominal ultrasonography, and chest roentgenogram until 1989; pelvic magnetic resonance imaging and chest CT were added thereafter.

Of the 44 patients for whom ASR was attempted, 40 received curative-intent ASR, and 4 received palliative-intent ASR because of 1 or 2 lung metastases in 3 and 3 liver metastases in 1. Of the 40 who received curative-intent ASR, 33 patients underwent macroscopic curative ASR, 2 with solitary liver metastasis underwent macroscopic curative ASR with complete resection of liver metastasis, 1 with 4 peritoneal metastases adjacent to the main tumor underwent macroscopic curative ASR with complete resection of peritoneal metastases, and the remaining 4 underwent palliative ASR because of macroscopic residual local tumor in 3 and residual lymph node metastases in 1. Of the four who received palliative-intent ASR, three with lung metastases underwent palliative ASR leaving only residual lung metastases in two and both residual lung and local tumors in one, and one with three liver metastases underwent

macroscopic curative ASR with complete resection of liver metastases. Consequently, 37 underwent macroscopic curative resection, and 7 underwent macroscopic palliative resection. Of them, 27 patients received no radiation, 13 received preoperative adjuvant radiation of 30 to 73 Gy (median, 44 Gy), and 4 received 44 to 50 Gy (median, 50 Gy) as previous treatment.

Data for these patients were collected and entered prospectively into the database of the Colorectal Surgery Division. They included the following: (1) patient demographics; (2) treatment and pathology of the primary rectal cancer; (3) presentation of PPR; (4) treatment and pathology of recurrent tumor; (5) operative details; (6) hospital course, including complications; and (7) outcome. Of these, 15 variables were selected for prognostic factor analysis (Table 1) by consideration of their potential relationship to survival after ASR, as indicated by previous studies.<sup>13-15,17-19,22</sup> The local disease-free interval (LDFI) was defined as the interval between the initial curative operation and the occurrence of symptoms or detection of asymptomatic PPR by CT.

### Surgical Procedure

Our surgical procedure was basically similar to that originally described by Wanebo and Marcove<sup>11</sup> and Wanebo et al.,<sup>13</sup> however, it was slightly modified.<sup>23</sup> Our sacral resection was performed immediately after the abdominal phase as a one-stage procedure instead of a two-stage procedure.<sup>13</sup> The presence of liver metastasis did not preclude continuation of the procedure if it was solitary and if the disease-free interval was sufficiently long. Solitary liver metastasis was resected simultaneously. We did not make full-thickness fascial myocutaneous flaps for sacroperineal wound closure but sutured the wound simply because there were no patients with large exposed tumors at the perineum.

After the patient was placed in a supine position with flexed and abducted thighs, dissection was started at the aortic bifurcation, and the common and external iliac vessels were dissected. The internal iliac vessels were divided at their root or beyond the superior gluteal artery. Adipose tissue, lymphatics, and the nodes surrounding these vessels, including obturator nodes, were removed completely, and the muscular pelvic side walls and the sacral nerve roots were exposed. The upper limit of the tumor was identified, and the anterior surface of the sacrum was dissected down to the planned level of sacral transection. When the tumor adhered or invaded into

TABLE 1. Univariate Predictors of Adverse Outcome

Variable	No. of Patients	Overall survival (%)			P
		1-yr	3-yr	5-yr	
Overall	44	90	47	34	
Gender					
Female	9	87	45	45	.41
Male	35	91	48	32	
Age					
< 60 years	30	96	55	40	.10
≥ 60 years	14	92	31	23	
Primary cancer stage					
I, II	2, 13	93	64	48	.046 (I, II, III vs. IV)
III	22	90	39	31	
IV	7	85	28	14	
Initial surgery					
Local excision, anterior resection	1, 20	90	51	36	.83
Abdominoperineal resection	23	90	44	34	
Initial lymphadenectomy					
Conventional	33	93	55	41	.25
Extended	11	81	27	18	
Local-disease-free interval (months)					
≤ 12	17	75	20	20	.0042
> 12	27	96	62	43	
Preoperative CEA level (ng/ml)					
≤ 10	23	91	70	49	.025
> 10	21	90	25	20	
Extent of preoperative pain					
None, perineum	15, 17	93	55	43	.0006 (none, perineum vs. buttock, more)
Buttock	7	85	35	0	
Thigh, leg	3, 2	50	0	0	
Tumor extent					
Solitary pelvic tumor	24	95	55	40	.17 (solitary tumor vs. others)
Pelvic metastasis	12	75	43	29	
Distant metastasis	8	85	28	28	
Largest tumor diameter (cm)					
≤ 5	26	92	50	40	.086
> 5	18	88	40	24	
Sacral involvement					
Adhesion	27	84	56	37	.85
Periosteum, marrow	11, 6	94	32	32	
Resection margin					
Microscopic negative	24	95	81	62	< .0001 (microscopic negative vs. others)
Microscopic positive	13	91	16	8	
Gross positive, residual	7	71	0	0	
Pathological grade					
Well, moderate	4, 29	90	40	35	.49 (poor, signet vs. others)
Mucinous, adenosquamous	6, 1	85	57	42	
Poor, signet-ring cell	3, 1	75	75	0	
Macroscopic growth pattern					
Solitary expanding	15	92	70	70	.0027 (solitary vs. others)
Multiple expanding	5	80	40	20	
Diffuse infiltrating	24	87	34	13	
Preoperative radiation					
Yes	13	91	55	46	.55
No	31	90	44	29	

CEA, carcinoembryonic antigen.

urogenital organs, the remaining rectum, pelvic nerves or muscles, and involved organs were all resected en bloc to avoid incomplete resection and cancer cell spillage. To facilitate resection and hemostasis and to shorten operating time, a combined abdominal and perineal approach was used.

After dissection of the lateral, cephalad, anterior, and caudal aspects of the tumor with surrounding organs to be resected was accomplished, the patient was placed in a prone position with flexed and abducted thighs. A posterior sacral incision including the perineal lesion was made, and the sacrum and

gluteal muscles were exposed. The gluteal muscles, sacrotuberous ligament, sacrospinous ligaments, and pyriformis muscles were divided as far from the tumor as possible. After the level of abdominal dissection and the extent of the tumor were confirmed by hand in the pelvic cavity, a laminectomy proximal to the planned level of sacral transection was performed to preserve the noninvolved sacral nerve roots and ligate the dura. The sacrum was transected by an osteotome, and en-bloc resection of the tumor with the sacrum and the surrounding organs was accomplished. The gluteal muscles and skin were closed primarily. Again, the patient was placed in a supine position with flexed and abducted thighs. A colostomy and an ileal conduit were made.

#### Extent of Resection

Levels of sacral transection included S2 in 6 patients, S2-3 in 19, S3 in 5, S3-4 in 11, S4 in 1, and S4-5 in 2. Thirty-nine patients underwent total pelvic exenteration, one underwent posterior pelvic exenteration, and four underwent abdominoperineal resection. En-bloc resection of entire pelvic lymph nodes with the bilateral internal iliac arteries and veins was performed for all patients. Resected organs included the rectum in 20 cases, the urinary bladder in 39, the uterus and vagina in 8, the external genitalia in 2, the obturator internus muscle in 12, the gluteus maximus muscle in 5, and the small intestine in 7. Urinary diversions were an ileal conduit in 37 patients and a ureterocutaneostomy in 2. Three patients underwent complete resection of one, one, and three synchronous liver metastases. In addition, one patient underwent complete resection of four peritoneal metastases.

#### Follow-Up

One patient returned to Indonesia and was lost to follow-up. The other 43 were followed up completely, with a median follow-up time for live patients of 4.7 years (range, 1.2-15.8 years). They were examined with abdominal and pelvic CT, chest roentgenogram or CT, and carcinoembryonic antigen (CEA) measurement every 4 months for 0 to 1 years, every 6 months for 2 to 4 years, and annually for 5 to 10 years.

#### Statistical Analysis

Survival, disease-free survival, and local disease-free survival distributions were estimated by using the Kaplan-Meier product-limit method. Univariate

comparisons of survival were made by using the log-rank test, and multivariate analysis was performed by using the Cox regression model with the forward stepwise method (likelihood ratio). All variables were dichotomized for analysis. Differences in proportions were analyzed by Fisher's exact test and by multivariate analysis with the logistic regression model and the forward stepwise method (likelihood ratio). All statistical analyses were performed with SPSS for Windows, version 10.0J (SPSS-Japan Inc., Tokyo, Japan). All *P* values were two sided, and a *P* value of <.05 was considered to be statistically significant.

## RESULTS

#### Pathologic Findings

Histological diagnoses of the PPR cases are listed in Table 1. The bone marrow or periosteum of the sacrum was histologically involved in 17 patients. The remaining 27 had no sacral invasion, but dense fibrotic tissues adhered extensively to the sacrum, and cancer cells were found within them. Of 13 patients with pelvic lymph node involvement, 12 had intrapelvic metastases alone, and 1 had both intrapelvic and extrapelvic metastases. Eight patients had distant metastasis, including liver metastasis in three, lung metastasis in three, peritoneal metastasis in one, and distant lymph node metastasis in one.

Resection margins were microscopically negative in 24 patients, microscopically positive in 13, macroscopically positive in 3, and grossly residual in 4 (lung, *n* = 2; lung and local, *n* = 1; lymph node, *n* = 1; Table 1). The sites of macroscopic positive margins included cut ends of the sacrum and/or presacral connective tissue in two, cut ends of the sacral nerves and the external iliac artery in one, and the lateral pelvic sidewall in one. The major artery was involved only in one patient with prior extended lateral pelvic lymph node dissection. The sites of microscopic positive margins included the cut end of the sacrum in two, the cut end of the presacral connective tissue in three, the cut ends of the sacrospinous ligament and sacrotuberous ligament in one, the cut ends of the sacrospinous ligament and obturator internus muscle in one, the cut end of the obturator lymph node in one, and the cut ends of the sacral nerves in one.

Macroscopic growth patterns were based on macroscopic views of sections of resected specimens and were classified as solitary expanding growth, multiple expanding growth, and diffuse infiltrating growth (Fig. 1; Table 1). Expanding growth featured smooth

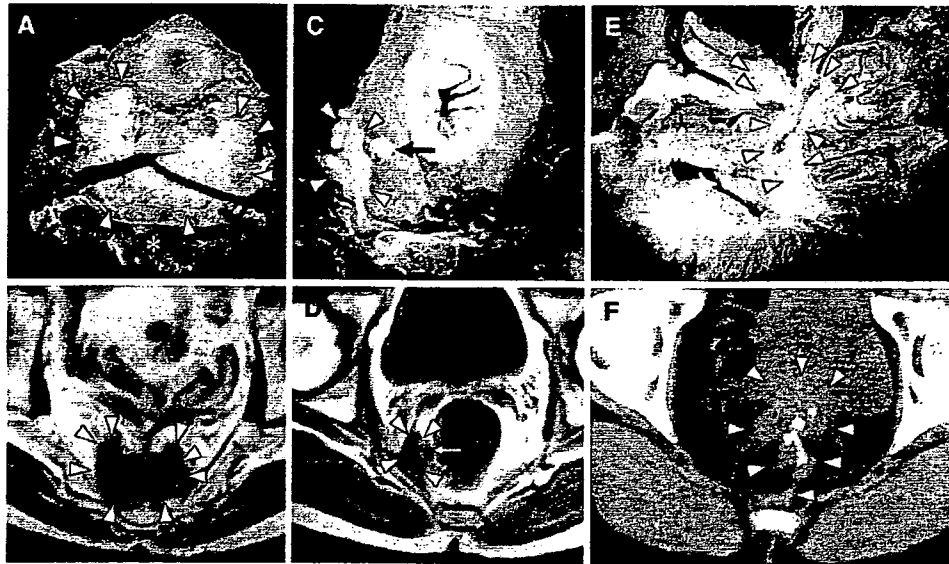


FIG. 1. (A) A section after abdominal sacral resection for posterior pelvic recurrence of rectal carcinoma. This tumor was macroscopically classified as solitary expanding growth. (B) Corresponding magnetic resonance image of (A). (C) A section of tumor macroscopically classified as multiple expanding growth. (D) Corresponding magnetic resonance image of (C). (E) A section of tumor macroscopically classified as diffuse infiltrating growth. (F) Corresponding computed tomography of (E). Arrowheads, main tumor; arrow, satellite tumor. \*Sacrum.

and clear margins. Any tumors showing irregular or obscure margins were therefore classified into the diffuse infiltrating category.

### Morbidity and Mortality

The median operating time was 751 minutes (range, 263–1377 minutes). The median blood loss was 3208 mL (range, 856–26160 mL), and all of the patients underwent transfusion. Of the 27 patients with postoperative complications (morbidity, 61%), 10 (23%) had major complications that necessitated surgical interventions or resulted in hospital death, and 17 (38%) had minor complications that could be managed conservatively (Table 2). The number of complications per patient was as follows: 4 in 1 patient, 3 in 5 patients, 2 in 10 patients, and 1 in 11 patients. One patient who had pelvic sepsis, residual tumor regrowth, bowel obstruction, and renal failure died on the 66th postoperative day (mortality, 2%).

Eleven (65%) of 17 patients who had received adjuvant or previous radiation had postoperative complications, compared with 16 (59%) of 27 who had not received radiation ( $P = .76$ ). In contrast, 7 (41%) of 17 with adjuvant or previous radiation experienced major complications, compared with 3 (11%) of 27 without irradiation ( $P = .03$ ). The median hospital stay was 38 days (range, 22–316 days).

TABLE 2. Complications

Complication	No. Patients
<b>Major complications</b>	
Pelvic sepsis	8
Bowel obstruction	3
Intestinal fistula	2
Ureteroileostomy leakage	2
Ureterocutaneostomy stenosis	1
Ileal conduit necrosis	1
Renal failure	1
Uncontrollable bleeding	1
Postoperative bleeding	1
Tracheal stenosis	1
<b>Minor complications</b>	
Wound dehiscence/infection	6
Bowel obstruction	12
Urinary tract infection	10
Ureteroileostomy stenosis	1
Neurogenic bladder	2

### Survival

The median survival for all the patients undergoing ASR was 2.3 years (range, .1–15.8 years). The estimated overall 1-, 3-, and 5-year survival rates were 90%, 47%, and 34%, respectively, including one hospital death (Fig. 2). Of the 15 patients who survived >4 years, 9 were disease free, and 5 survived >8 years. The disease-free 1-, 3-, and 5-year survival rates were 44%, 26%, and 24%, respectively. The local disease-free 1-, 3-, and 5-year survival rates were 63%, 47%, and 47%, respectively (Fig. 2).

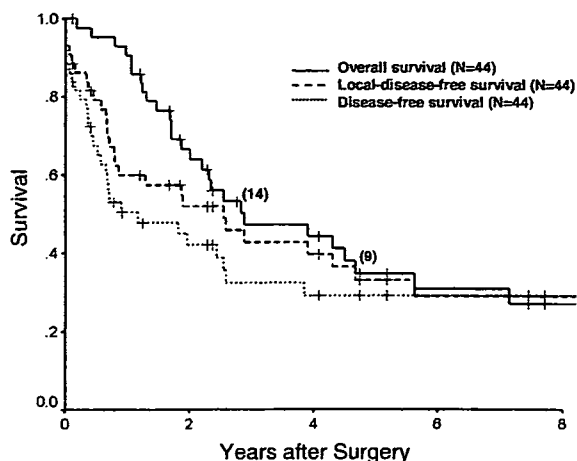


FIG. 2. Overall, disease-free, and local disease-free survival distributions for the 44 patients undergoing abdominal sacral resection for posterior pelvic recurrence of rectal carcinoma. The numbers in parentheses for the overall survival curve indicate the patients alive at 3 and 5 years.

**Prognostic Factors**

Results of univariate analysis of prognostic factors are summarized in Table 1. The overall survival of the patients with microscopic positive resection margins was significantly worse than that of those with microscopic negative margins ( $P < .0001$ ) but was not significantly better than that of those with macroscopic positive margins or macroscopic residual tumor ( $P = .11$ ). Patients with macroscopic positive margins or macroscopic residual tumor did not survive  $> 2.3$  years.

The survival of patients with buttock pain was significantly worse than that of those without pain or with perineal pain ( $P = .043$ ) and was significantly better than that of those with thigh or leg pain ( $P = .0046$ ). The latter died within 1.2 years.

Of the eight patients with distant metastasis, two undergoing resection of solitary liver metastasis were alive and disease free for 7.6 and 2.7 years, one undergoing resection of three liver metastases died of disease at 1.3 years, one undergoing resection of four peritoneal metastases was alive with disease at 1.1 years, three with one or two lung metastases died of disease at 2.3, 2.0, and 1.6 years, and one with para-aortic lymph node metastasis died at 1.7 years.

The univariate analysis of the 15 variables (Table 1), when dichotomized, showed a positive resection margin, pain extending to the buttock or further, multiple growths or diffuse infiltrating growth, LDFI of  $< 12$  months, a preoperative CEA level  $> 10$  ng/mL, and primary cancer stage IV to be

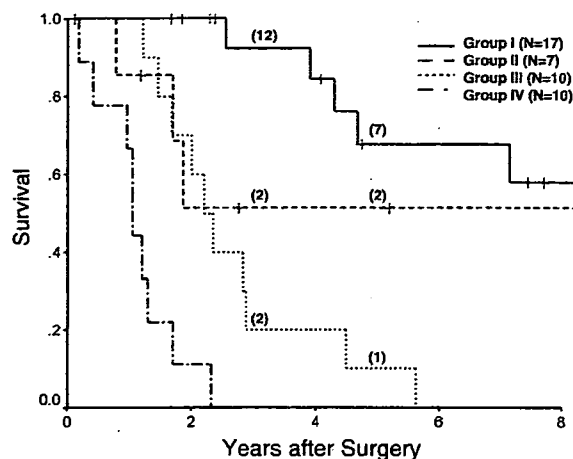


FIG. 3. Overall survival curves for group I (microscopic negative margin and local disease-free interval [LDFI] of  $> 12$  months), group II (microscopic negative margin and LDFI  $< 12$  months), group III (positive margin and LDFI  $> 12$  months), and group IV (positive margin and LDFI  $< 12$  months). The numbers in parentheses for each curve indicate the patients alive at 3 and 5 years.

associated with significantly worse survival. The other nine factors did not show any significant association with outcome.

The multivariate analysis of the 15 dichotomized variables revealed that only a positive resection margin (hazard ratio, 10 [95% confidence interval, 3.8–28];  $P < .001$ ), an LDFI of  $< 12$  months (4.2 [1.8–9.8];  $P = .001$ ), and pain radiating to the buttock or further (4.2 [1.6–11];  $P = .004$ ) were independently associated with worse survival.

When the most significant independent factors were considered together, the 5-year overall survival rates of the 17 patients with microscopic negative margins and an LDFI  $> 12$  months (group I), the 7 with microscopic negative margins and an LDFI  $< 12$  months (group II), the 10 with positive margins and an LDFI  $> 12$  months (group III), and the 10 with positive margins and an LDFI  $< 12$  months (group IV) were 67%, 51%, 10%, and 0%, respectively (Fig. 3). There were significant survival differences between group I and group III ( $P < .0001$ ), group III and group IV ( $P = .0014$ ), and group II and group IV ( $P = .01$ ). Group IV patients did not survive  $> 2.3$  years.

**Risk Factors for a Positive Resection Margin**

To clarify the risk factors for a positive resection margin, the most significant prognostic factor on multivariate analysis, univariate and multivariate analyses were conducted. Three patients who under-

TABLE 3. Univariate predictors of positive resection margin

Variable	Microscopic margin		P
	Negative	Positive	
Gender			
Female	5	3	1.0
Male	19	14	
Age, years			
< 60	19	10	.18
≥ 60	5	7	
Primary cancer stage			
I/II/III	23	12	.066
IV	1	5	
Initial surgery			
Local excision, anterior resection	13	8	.76
Abdominoperineal resection	11	9	
Lymphadenectomy at initial surgery			
Conventional	20	13	.70
Extended	4	4	
Local-disease-free interval (month)			
≤ 12	7	9	.20
> 12	17	8	
Preoperative CEA level (ng/ml)			
≤ 10	16	6	.062
> 10	8	11	
Extent of preoperative pain			
None, perineum	21	9	.029
Buttock, thigh, leg	3	8	
Tumor extent			
Solitary pelvic tumor	17	7	.11
Pelvic metastasis, distant metastasis	7	10	
Largest tumor diameter (cm)			
≤ 5	15	9	.75
> 5	9	8	
Sacral involvement			
Adhesion	14	11	.75
Periosteum, marrow	10	6	
Pathological grade			
Well, moderate, mucinous, adenosquamous	21	16	.63
Poor, signet-ring cell	3	1	
Macroscopic growth pattern			
Solitary expanding	12	2	.018
Multiple expanding, infiltrating	12	15	
Preoperative radiation			
Yes	8	3	.31
No	16	14	

CEA, carcinoembryonic antigen.

went palliative-intent resection as a result of gross residual lung metastases were excluded from this study. Univariate analysis revealed that the incidences of microscopic positive margins were significantly higher in patients with multiple expanding or diffuse infiltrating growth (56% vs. 14%;  $P = .018$ ) and in patients with pain extending to the buttock or further (72% vs. 30%;  $P = .029$ ; Table 3). On multivariate analysis of the 14 dichotomized variables, excluding resection margin, multiple expanding or diffuse infiltrating growth was independently associated with positive margin (hazard ratio, 7.5 [95% confidence interval, 1.4–40];  $P = .019$ ).

TABLE 4. Sites of first recurrence after abdominal sacral resection in 37 patients undergoing macroscopic curative resection

Site	No. Patients (%)
Local	
Local alone	6 (24)
Local, lung	3 (12)
Local, adrenal gland	1 (4)
Local, lung, liver	1 (4)
Local, lung, pancreas	1 (4)
Local, liver, para-aortic lymph node	1 (4)
Lung	
Lung alone	5 (20)
Lung, para-aortic lymph node	2 (8)
Liver, lymph node	1 (4)
Para-aortic lymph node	1 (4)
Peritoneum	1 (4)
Brain	1 (4)
Unknown	1 (4)

#### Recurrence Patterns

Of the 37 patients who underwent macroscopic curative resection, 25 (68%) experienced further recurrence. Sites of their first recurrence after ASR are listed in Table 4. Of them, 13 patients (52%) had local failure, 7 (28%) had lung metastasis, and 14 (56%) had failures confined locally or to the lung. Sites of local failure were the cut end of the sacrum in five, the sacral cut end and buttock in one, and the pelvic side wall or ischium in 3. None of the 25 patients with recurrence was treatable by surgery, so these patients were given chemotherapy, radiotherapy, and/or best supportive care.

Of the 13 patients who developed local failure, 9 had positive margins, and 4 had negative margins on histological analysis. Of the 24 patients without local failure, 20 had microscopic negative margins, and 4 had microscopic positive margins. The rate for local failure was significantly higher in patients with microscopic positive margins than in those with microscopic negative margins (69% [9 of 13] vs. 17% [4 of 20];  $P = .003$ ). When the accuracy of the microscopic status of surgical margins in prediction of local failure was evaluated, the sensitivity was 69% (9 of 13), the specificity was 83% (20 of 24), the positive predictive value was 69% (9 of 13), the negative predictive value was 83% (20 of 24), and the overall accuracy rate was 78% (29 of 37). Of the 13 patients with microscopic positive margins, 9 developed local recurrence that corresponded well to histological findings, 1 experienced local failure at a different site with a positive margin, and 3 had no obvious local failure at the last follow-up.

## DISCUSSION

The most effective treatment for PPR of rectal carcinoma is a curative resection, that is, complete resection with microscopic negative margins.<sup>13,15,17-19,22</sup> Because the tumor involves contiguous organs, including the sacrum, retained rectum, internal iliac vessels, and genitourinary organs, by either invasion or dense adhesion, combined resection of these organs—that is, ASR—is mandatory for clear surgical margins and possible cure. The overall 5-year survival rate after ASR is reported to be 25% to 31% in the largest series<sup>13,14</sup> and was 34% in this study. Such results have never been achieved with other therapeutic modalities, including chemotherapy and radiotherapy.<sup>4-9</sup>

However, morbidity and mortality after ASR are reported to be 26% to 82%<sup>13,15-18,21,22</sup> and 0% to 9%,<sup>13-22</sup> respectively. In our series, they were 61% and 2%, and 23% of our patients experienced major complications resulting in reoperation or death, and their mean hospital stay was 135 days. In addition, most patients lose genitourinary functions and must endure permanent stomas. These costs are very high and sometimes even catastrophic for those who nevertheless do not obtain long-term survival. Therefore, appropriate patient selection based on survival benefit determined on the basis of prognostic factors is necessary. Also, efforts toward seeking effective adjuvant therapy aiming at the most common sites of recurrence are mandatory. Thus, we analyzed prognostic factors and recurrence patterns after ASR in this study.

Several factors that can be estimated before surgery have been reported to be significantly associated with prognosis on either univariate or multivariate analysis. These include residual tumor extent,<sup>13,15,17-19,22</sup> distant metastasis,<sup>14</sup> initial operation,<sup>13</sup> disease-free interval,<sup>14</sup> preoperative CEA level,<sup>13,14</sup> preoperative CEA doubling time,<sup>14</sup> and proliferating cell nuclear antigen labeling index.<sup>24</sup> In addition, whether significant or not, there are factors definitely indicative of a poor prognosis. Wanebo et al.<sup>13,25</sup> reported that patients with positive margins, bone marrow involvement, or pelvic lymph node involvement had a median survival of only 10 months. Strong suspicion of such factors thus contraindicates ASR. However, the number of patients so far studied is still not sufficiently large to allow definitive patient selection criteria to be established.

We tested 15 factors in multivariate analysis because previous studies indicated their potential relationship to survival after ASR.<sup>13-15,17-19,22,24,25</sup> Of

these, microscopic positive margins, LDFI < 1 year, and preoperative pain exceeding the buttock showed a significant independent association with a poor prognosis. Microscopic margin status is the most significant, as reported so far.<sup>13,15,17-19,22</sup> Of our patients with microscopic positive margins, 69% developed local recurrence, and this caused persistent pain and a poor prognosis. Although some previous studies claimed a benefit of palliative resection for both survival and pain,<sup>26</sup> it usually leads to a very poor prognosis and fails to relieve pain, as previously reported.<sup>25,27</sup> Therefore, palliative resection leaving a gross residual tumor should not be attempted. In addition to conventional imaging,<sup>28,29</sup> recent advances in radiological imaging, including thin-section magnetic resonance imaging<sup>30</sup> and multidetector row CT,<sup>31</sup> allow us to accurately evaluate tumor extent so that cautious interpretation can preclude such unnecessary surgery.

The extent of preoperative pain corresponds well with tumor extent and invasiveness and therefore predicts survival.<sup>17</sup> In this study, the survival of the patients with buttock pain was significantly worse than that of patients without pain or with perineal pain and was significantly better than that of patients with thigh or leg pain. Thigh or leg pain, caused by involvement of the first or second sacral nerves, indicates lateral and/or cephalad extension of the tumor, which usually renders curative resection impossible. Indeed, in our series, the affected patients died within 1.2 years. In contrast, if the pain remains within the buttock, there is the possibility of curative resection.

The factors relating to tumor growth rate can predict prognosis only if patients have residual tumors after ASR. Maetani et al.<sup>14</sup> and Onodera et al.<sup>24</sup> reported a significant association of disease-free interval<sup>14</sup> and preoperative CEA doubling time<sup>14</sup> with survival. These parameters reflect not only the growth rate of locally recurrent tumors, but also that of distant metastases. The proliferating cell nuclear antigen labeling index<sup>24</sup> can reflect a growth rate specific to local recurrence, so it may predict prognosis more accurately. Although LDFI has not been studied so far, it is easier to measure than the labeling index, and it is also specific to local recurrence. As this study showed, patients with an LDFI of > 12 months and clear surgical margins are the best candidates for ASR, and a 5-year survival of 67% can be expected. Conversely, if the LDFI is < 12 months, thus indicating rapid tumor growth, and resection is palliative, a 2-year survival of only 11% is expected. In such cases, ASR should not be attempted. Pallia-

tive resection is indicated only for patients with an LDFI of > 12 months and preferably > 18 months.<sup>11</sup>

Primary cancer stage, preoperative CEA level, and macroscopic growth pattern were prognostically significant only in univariate analysis in this study. Thus, they are related to any of the previously described independent factors, but they are worth considering to a certain degree when decisions are made. Macroscopic growth pattern, which has not been investigated so far, especially influences the surgical margin status and is important when deciding the extent of resection.

As our logistic regression model showed, multiple expanding or diffuse infiltrating growth is independently associated with positive resection margins. The curative resection of the tumors with multiple expanding or infiltrating growth (44%) is clearly more difficult than with solitary expanding growth (86%). Therefore, cautious evaluation of both growth pattern and tumor extent by magnetic resonance imaging or CT is needed to determine a correct line of resection.

Although tumor extent (distant and pelvic metastases)<sup>14,25</sup> and initial operation type<sup>13,25</sup> have been reported to be significant prognostic factors, this was not confirmed here, presumably at least partly because of differences in patient backgrounds and selection criteria. As described previously,<sup>11</sup> the presence of pulmonary, multiple liver, peritoneal, and extrapelvic lymph node metastases leads to a very poor prognosis, with a median survival of only 1.6 years in our cases, so these patients should not undergo ASR. However, solitary liver metastasis may be an exception. Indeed, in our series, two patients with solitary liver metastases survived disease free for 7.6 and 2.7 years after ASR and liver resection. In such cases, aggressive surgery seems justified.

Because adjuvant external beam radiotherapy has been reported to be beneficial for local control and prolongation of survival in primary rectal carcinoma,<sup>32,33</sup> many surgeons have recommended its application for ASR.<sup>13,15-18,20</sup> In this multivariate study, however, a prognostic benefit of preoperative radiotherapy could not be detected. This may be at least partly caused by the small number of patients, so further investigation is necessary. Marijnen et al.<sup>34</sup> reported that preoperative radiotherapy for primary rectal cancer has a beneficial effect in patients with more than 1-mm resection margins but that it cannot compensate for microscopically nonradical resection resulting in positive margins. Therefore, preoperative radiation should be given only to patients for whom surgical margins are expected to be attained but insufficient.

The situation with intraoperative radiotherapy may be different.<sup>13,15-17</sup> Hahnloser et al.<sup>17</sup> reported that the overall 5-year survival rate of patients undergoing palliative resection and intraoperative radiotherapy with or without external beam radiotherapy was 21%. Survival rates for their patients with no fixation, one fixation, two fixations, and three or more fixations were 43%, 24%, 20%, and 0%, respectively. Although candidates for ASR usually have two or more fixations and the expected survival of those with positive margins is not good, intraoperative radiotherapy may benefit those undergoing ASR despite a positive margin.

As to recurrence patterns after ASR, this study showed that, in 56% of our patients, recurrence was confined locally or to the lung. Wanebo et al.<sup>13</sup> reported this to be the case for 68% of their series, in line with other previous studies.<sup>35,36</sup> Thus, in addition to precise resection based on precise evaluation of tumor extent with thin-section magnetic resonance imaging or multidetector row CT, adjuvant therapies aiming at local and lung recurrences may be necessary. For local control, preoperative and intraoperative radiotherapy may be helpful. For lung metastases, systemic adjuvant chemotherapy using 5-fluorouracil-based chemotherapy or newly developed drugs (or their combination) may be effective.<sup>5,6</sup>

Although this retrospective exploratory study featured only a relatively small number of patients, we conclude that ASR is beneficial for a selected subset of patients in terms of survival prolongation and even cure. To select appropriate patients, evaluation of resection margin, LDFI, pain extent, and growth pattern is important. To improve survival, adjuvant treatment should be aimed at local and lung recurrences.

#### ACKNOWLEDGMENTS

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## 腫瘍外科治療の最前線

## D. 大腸・肛門の腫瘍性疾患

## 34. 早期大腸癌

## -EMR, 鏡視下手術の対象となるもの-

*Early colorectal carcinoma : The indication of endoscopic resection and laparoscopic surgery*

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遠隔転移を伴わない、大腸早期癌の治療に関して概説した。治療法の選択には深達度診断が必要であり、内視鏡による観察と適切な部位からの生検が重要である。粘膜下層深層までの浸潤がある場合、あるいは内視鏡的切除した標本の組織学的検討により危険因子が認められた場合には、腸管切除+リンパ節郭清の適応であり、大部分の症例で腹腔鏡下手術が可能である。手術に際しては、リンパ節転移の危険があるための手術であり、切除標本に癌組織が存在しない場合があることを十分説明し、理解を得ておくことが必要である。

key word 早期大腸癌/EMR/ESD/腹腔鏡/リンパ節転移



## 疾患の概念

大腸早期癌とは、深達度が粘膜下層までにとどまる大腸癌のことを指す。転移の有無は問わないので、リンパ節転移を伴っている場合でも、深達度が粘膜下層までであれば、早期癌に分類される。頻度は低いが、「遠隔転移を伴う早期癌」も存在する。本稿では、内視鏡的切除および鏡視下手術の対象となる大腸早期癌を取り扱うので、遠隔転移を伴う早期癌は除外する。

早期癌の中には、深達度が粘膜内にとどまるものと、粘膜下への浸潤を伴うものがあるが、粘膜内癌は決して転移することがない。「転移する能力があること」が悪性であるという立場からは、したがって粘膜内癌は癌ではないともいえる。欧米ではこのような考えから、粘膜下への浸潤をもって癌と診断することが一般的である。

一方本邦では、細胞異型および構造異型により腫瘍の質的診断を行うのが一般的であり、粘膜下層へ

の浸潤の有無は癌と診断するための条件とはされていない。

粘膜内癌は、「癌」ではあるが、腫瘍自体を切除することにより根治が可能で、再発の危険もない。臨床的には「良性」腫瘍と同じ取扱いでかまわない。大腸癌治療ガイドライン医師用2005年版によると、粘膜下層浸潤癌では、9.9%にリンパ節転移が認められる。粘膜下層浸潤癌のうちの多くは、内視鏡的に切除が可能であり、リンパ節転移がないのであれば、内視鏡的切除で治療は終了となる。

一方、仮にリンパ節転移があるにもかかわらず内視鏡的切除のみしか行わなかった場合、残存したリンパ節転移が増殖・転移し、手術を行っていれば根治できた症例が、死の転帰をとることになる。かといって、内視鏡的切除後の組織学的診断で粘膜下層への浸潤が認められた場合に、ことごとく外科手術を追加した場合、まったく癌の存在しない部位の切除が数多く行われてしまう。「癌細胞がない部位を切除する」という意味で「無駄な」手術(和製英語であるが、“oversurgery”)を減らし、一方でリンパ節転

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移例に関しては遺漏なく手術を行う。それが早期大腸癌の治療のポイントとなる。

## 臨床診断・画像診断・病理所見上の特徴

### 1. 臨床診断

早期大腸癌が症状を呈することはまれであり、その意味では問診から身体診察に至る過程で早期大腸癌が診断されることは通常ない。例外として、下部直腸に腫瘍が存在する場合には直腸指診で触知されることがあり、時にはいきみにより肛門から脱出して発見されることもある。実際の診断の契機は、非特異的な症状に対して行われた検査、あるいは検診で異常を指摘されたため施行された検査がほとんどである。別に進行癌(深達度が固有筋層以深の癌)があり、全大腸内視鏡検査を行った際に同時性病変として認められることもある。

### 2. 画像診断

画像診断の方法としては、注腸造影検査と大腸内視鏡検査が広く用いられている。従来は、注腸造影検査がスクリーニングとして行われ、注腸造影検査で異常所見が認められた場合に大腸内視鏡検査を行うことが一般的であった。しかし、近年では、大腸内視鏡検査の診断能が向上し、機器の進歩により挿入が比較的容易となったこと、また存在診断とともに、組織学的診断が可能で、時には治療(内視鏡的切除)まで行うことができることから、両検査の位置づけは変化しつつある。次第に、第一選択が大腸内視鏡検査となりつつあり、その後必要な場合に注腸造影検査を行うようになってきている。当科では、現在でも必要な場合には注腸造影検査を行っているが、腫瘍の質的診断に関しては、注腸造影検査の追加で得られる情報はほとんどなく、主として内視鏡で部位を診断しにくい場合に部位の確認に有用であると考えている。

大腸内視鏡検査で重要なことは、まず腫瘍自体の存在を認識することで、腸管内の残渣を良く吸引すること、襞の裏側を丁寧に観察することが基本となる。早期大腸癌の多くの割合を占める隆起性病変の存在診断は、このような丁寧な観察で比較的容易に可能である。

一方、平坦型病変の場合には、大腸壁の凹凸にだけ注目すると診断されないことがあり、淡い色調の変化や血管紋理の途絶に留意する。また、腫瘍に随伴する変化である白斑が腫瘍よりも先に認識されることがある。白斑を見たら周囲に腫瘍がある可能性が高いので注意深く観察する。

存在診断の後は、質的診断を行う。通常観察では、①深い陥凹、②不自然な凹凸、③白苔、④不自然な髪集中、⑤易出血性、⑥緊満感、⑦空気変形が深達度と関連する所見である。

それぞれの所見の有無の判定には主観が入り、またこれら所見のうちいくつか陽性であればどれだけの確率で深達度が推定される、という数式があるわけではない。所見の見分け方、判断時における所見の意義づけの軽重など、「経験がものを言う」部分も多い。当科での検討では、これら通常観察による粘膜下層浸潤度診断の正診率は74%であった。

通常観察の後に、拡大観察を行う。拡大観察は、従来腺管の開口部の分布パターンを診断することが広く行われており、拡大観察=ピットパターン診断といえる状況であったが、近年、NBI(Narrow Band Imaging)機器が開発され、腫瘍表面の血管パターンを読むことも盛んに行われている。詳細は本稿の範囲を超えるので、ここではピットパターン診断に関して簡単に述べる。インジゴカルミンあるいはクリスタルバイオレットを散布した後に拡大観察を行うことにより、腺管開口部の分布パターンが詳細に観察される。パターンは数種類に分類されているが、重要なのは、癌が浸潤することにより表層の粘膜固有層が剥落し、癌の浸潤した粘膜下層が露出した状態を捉えることである。このような状態では、「腺管の開口部」は存在せず、無構造な局面が認められる。これは  $V_N$  ピットと言われており、Nは non-structure の頭文字とされている。このような無構造局面が確認された場合、粘膜下層への浸潤距離は  $1,000 \mu\text{m}$  を超える場合がほとんどである。この  $1,000 \mu\text{m}$  の意義に関しては後述する。「無構造」な表面の質感は、必ずしも拡大内視鏡でなくとも捉えられることがあり、通常内視鏡を用いた場合でもできるだけ近接して細かな所見をみるようにする。

腫瘍最深部を標的とした生検により、癌が腺腫かに加えて、癌の場合の浸潤度が評価可能な場合もあ

## MEMO 1

## 大腸生検のグループ診断

生検診断は、正常組織(Group 1)、異形があるが非腫瘍(Group 2)、腺腫(Group 3)、癌が疑われる腫瘍(Group 4)、癌(Group 5)と分類されている(大腸癌取り扱い規約)。治療の面からは、粘膜下層深部まで浸潤した像が生検から確認できれば、リンパ節郭清を含む腫瘍学的切除の適応であると判断できるが、そのような「より高度のGroup」は定義されていない。一方、国際的な分類であるウィーン分類では、GroupではなくCategoryという用語を用いているが、非浸潤癌(Category 4)と浸潤癌(Category 5)を分けて定義している。

## MEMO 2

## 間質反応(desmoplastic reaction)

粘膜下層に浸潤する癌腺管の周囲に反応性に認められる膠原繊維の増生を間質反応(desmoplastic reaction)という。粘膜固有層が癌の浸潤に伴い、剥落すると粘膜下層が表面に露出するので、このような部位から生検を行うと、生検標本上で間質反応が確認できる。間質反応が確認できた場合には高率で、粘膜下層深層までの浸潤病変であると診断できる。一方、生検部位が適切でない場合や、表面構造が保たれたまま癌が粘膜下層に浸潤している場合には、生検で間質反応を確認することはできない。したがって、生検による間質反応所見は、粘膜下層深部浸潤に関して、陽性的中率は高いが、陰性的中率は低いと考えられる。

る。癌の粘膜下層への浸潤により粘膜固有層が剥落し、癌が浸潤した粘膜下層自体が採取されることもある。「グループ」を用いた生検診断では、グループ5すなわち癌としか診断されないが、生検標本で間質反応が確認できれば、さらに進んで「浸潤癌」との診断が可能である。この所見が生検で認められた場合には、粘膜下層への深部浸潤があると判断してよく、内視鏡的切除は適応とならない。

注腸造影検査で大腸内視鏡検査を上回る情報を得ることは困難である。腫瘍の側面像を捉え、壁変形の有無と程度を評価することで、深達度診断を行うことができる。無変形、角状変形、弧状変形がそれぞれ粘膜内に限局、わずかに粘膜下層に浸潤、粘膜下層深層まで浸潤にそれぞれ対応するとされている。ただし、大腸の壁自体にも弧状の変形があり、その解釈は時に困難である。

内視鏡的切除で得られた原発巣を検討することにより、リンパ節転移のリスクを評価することは非常に重要であり、病理組織学的あるいは分子生物学的アプローチがなされている。多数の因子がリンパ節転移と相関すると報告されているが、現在一般的に用いられているのは、①1,000  $\mu\text{m}$  以上の粘膜下層への浸潤、②脈管侵襲、③低分化が、リンパ節転移と相関することである。これら3条件のどれにも該当しない場合には、リンパ節転移の危険が低く、内視鏡的切除により治療を完了してもよい、とされている。



### 発育・進展形式、再発形式

大腸癌には、腺腫を経て癌化するものと、腺腫を経ず、初めから癌として発生するものがある。また、隆起性に発育・進展するものが多いが、一部、浸潤性発育が主体で、隆起成分が少ない病変もある。多段階の遺伝子変異、あるいは遺伝子発現の変化がどのような順番で、どのような間隔でおこなうかによりこれらの性質が決定されると考えられる。

再発形式は、リンパ節再発、血行性転移再発がある。腹膜播種性再発は、原発巣が粘膜下層までに限局していることから、きわめてまれと考えられる。



### 治療方針と治療の実際

治療法には、内視鏡的治療と外科的治療がある。内視鏡検査の際に、深達度が粘膜下層浅層(1,000  $\mu\text{m}$  以下)までであると診断した場合には、リンパ節転移の可能性がきわめて低い。したがって、技術的に切除が可能であれば、内視鏡的切除を行う。そのうえで、前述した3条件に合致するかどうかを組織学的に確認し、外科的治療の適応を決定する。

一方、深達度が粘膜下層深層に至っていると診断された場合には、外科的治療の適応とすることが一般的である。ただし、内視鏡的深達度診断が必ずしも組織学的深達度診断と一致しないこと、および近年内視鏡的切除の技術レベルがめざましく向上していることから、技術的に完全切除が可能であると考えられる場合には、組織学的確診を得る目的で、内

視鏡的切除を行う選択もある。内視鏡的深達度診断の確実性と、内視鏡的切除の難易度とを考慮して適応を決定することになるが、ESD関連の技術および機器の進歩により、以前であれば内視鏡的切除を行わないような病変に対しても、積極的に内視鏡的切除を行う傾向がある。内視鏡的切除後に組織学的所見を確認して、外科的切除の適応を決定することは前項と同様である。

外科的治療は、原発巣の切除とリンパ節郭清からなる。内視鏡的には粘膜下層への浸潤はないが、技術的に切除が困難で外科的治療の適応となった症例に関しては、あえて広範囲のリンパ節郭清を行う必要はない。内視鏡的切除を行い、リンパ節転移のリスクがあると判断された場合には、上腸間膜動脈系ではD2、下腸間膜動脈系ではD1+242ないし232番リンパ節郭清を行っている。内視鏡的切除を行わず、外科的手術を行う場合には、原則は内視鏡的切除後の症例と同様であるが、深達度が粘膜下層を超えている可能性を考えるべき病変であれば、下腸間膜動脈系でもD2を施行している。

外科的治療のアプローチ法としては、開腹手術と腹腔鏡補助下手術がある。アプローチ法により切除範囲を変更することはない。短期成績に関しては、腹腔鏡補助下手術の方が疼痛が軽度で、術後の回復が早いことが示されている。長期成績に関しては、スペインおよび米国から無作為化試験が報告されている。対象は進行癌が主体であるが、アプローチ法による長期成績の差はないようである。本邦でも、進行癌を対象としたものであるが、腹腔鏡下手術と開腹手術の成績を比較するRCTが行われており、2007年1月現在で、予定症例数の半数の登録が終了している。腹腔鏡補助下手術は、開腹手術と比較して技術的に困難であり、病変の部位に加えて、肥満度や開腹手術既往の有無・種類の影響も大きい。手術時間が長くなること、および通常行われる気腹が循環呼吸器系に負荷となることも、アプローチ法を決定する際に考慮する必要がある。

当科では、早期癌に対しては原則として腹腔鏡補助下手術を第一選択とし、循環器・呼吸器合併症がある症例の場合は、各専門医へのコンサルトを行った上で個別にアプローチ法を決定している。

下部直腸に病変が存在する場合には、①手術侵襲

が大きく、②術後機能障害が出現する可能性があること、および③経肛門的、経仙骨的なアプローチ、あるいはTEMによる切除が可能であること、という特殊性を考慮する必要がある。とくに、原発巣が内視鏡的節切除を行った後にリンパ節転移の危険因子が認められたため手術を行う場合には、切除標本内に癌組織が認められない場合の方が多いためであるから、術前に十分なインフォームドコンセントが必要である。経肛門的切除、経仙骨的切除などの局所切除では、十分なリンパ節郭清ができず、近年の内視鏡的切除の進歩により適応は縮小しつつある。

### 治療成績と予後

粘膜内病変およびリンパ節転移の危険因子を有さない粘膜下層浸潤癌は、局所のコントロールにより完治する。当科で加療した大腸SM癌198例のうち、再発が認められた症例は3例(1.5%)で、うち2例が肝転移(いずれも外科的切除を行い、その後無再発)、1例が傍大動脈リンパ節であった。大腸癌治療ガイドライン医師用2005年版によると、大腸SM癌の再発率は1.3%(9/715)と報告されている。

### ICの進め方・要点など

図1に沿って説明する。大腸内視鏡で腫瘍が認められた場合、内視鏡的切除の適応の決定が必要である。浸潤が粘膜内あるいは粘膜下層浅層までにとどまると判断され、技術的に可能であると考えられれば、内視鏡的切除を行う。この際、内視鏡的切除の手技とその危険性に関して説明を行う必要がある。また、内視鏡的切除を試みても、改めて行った観察や、途中の段階の所見で切除不能と判断され、中止する可能性があることも併せて説明する。中止の説明があらかじめ行われていないために、完全切除ができないことを認識しつつ、危険かつ不必要な内視鏡的切除を、「社会的必要性」から、あるいは「ポーズ」として行うようなことがあってはならない。

内視鏡的切除した標本の組織学的所見から、リンパ節転移の危険因子が確認された場合、追加腸切除を行うことに関して、説明が必要となる。①危険因子がある場合に実際にリンパ節転移が存在する確率

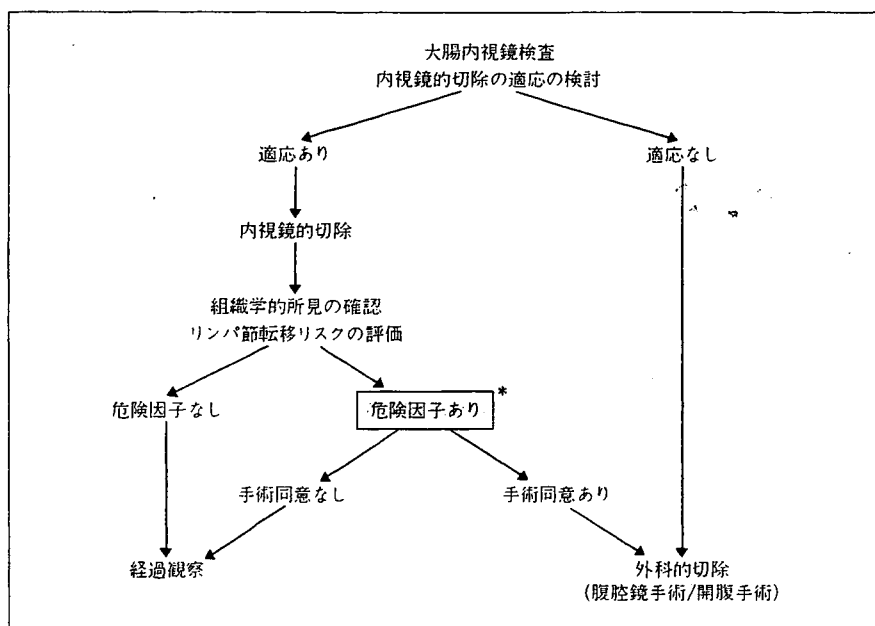


図1 大腸早期癌の治療の流れ

は、10～15%程度と考えられ、それ以外の症例では手術を行っても切除標本内に癌組織は認められないこと、②一方、この確認は手術を行い、切除標本を組織学的に検索してはじめて可能になること、③手術には苦痛と危険が伴うこと、がポイントとなる。当科で、リンパ節転移の危険因子がある、と判定された場合には、手術を受けることを推奨しており、大部分の症例に対して追加腸切除+リンパ節郭清を行っている。少数の手術拒否例ではこれまで幸いにして再発は認められていないが、リンパ節再発が画像検査で確認された時点で手術を行った場合の長期成績は明らかでない。内視鏡的切除後すみやかに追加腸切除を行った場合の再発率は、当科の成績では6.7%(1/15)と低く、明らかなリンパ節再発が認めら

れた後に手術を行った場合、十分なデータはないが、再発率がこれより高いことが推定される。したがって、「自己決定権」は最大限尊重すべきであるが、安易な「患者まかせ」ではなく、医療側のはっきりとした姿勢(この場合、追加腸切除の推奨)を示す必要があると考える。

手術を行った後、リンパ節転移が認められた場合には、病期 III となるので、補助化学療法の適応である。補助化学療法に関しても、①体内に潜在的な転移がある可能性があること、②それに対して補助化学療法を行うことで、一部の症例で再発が予防できること、を説明する。病期 III で無治療群と補助化学療法群を比較した RCT の結果から外挿すると、再発症例のうち1/3程度で再発が予防できるようである。

# Histological identification of fascial structures posterolateral to the rectum

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**Background:** A comprehensive understanding of fascial structures around the rectum is important for surgeons. Multilaminar fascial structures have provided different interpretations of reliable surgical planes in rectal surgery.

**Methods:** Pelvic visceral materials for histological assessment were obtained from 12 male cadavers. Large specimens covering wide areas around the mesorectum were embedded in paraffin, followed by preparation of semiserial horizontal sections and sagittal sections for histological examination.

**Results:** Histological examination demonstrated a prehypogastric nerve fascia and parietal presacral fascia in the retrorectal multilaminar structure. The parietal presacral fascia seemed to divide into several lateral continuations. The prehypogastric nerve fascia appeared to join the most medial continuation of the parietal presacral fascia, which continued ventrally and communicated with Denonvilliers' fascia. Any fascial structure connecting directly between the fascia propria of the rectum and the parietal presacral fascia (that is, the rectosacral fascia) was not found in sagittal sections.

**Conclusion:** In the retrorectal multilaminar structure, prehypogastric nerve fascia is evident between the fascia propria of the rectum and the parietal presacral fascia. Sharp dissection in front of the prehypogastric nerve fascia according to the histological configuration of the posterolateral fasciae seems reliable.

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## Introduction

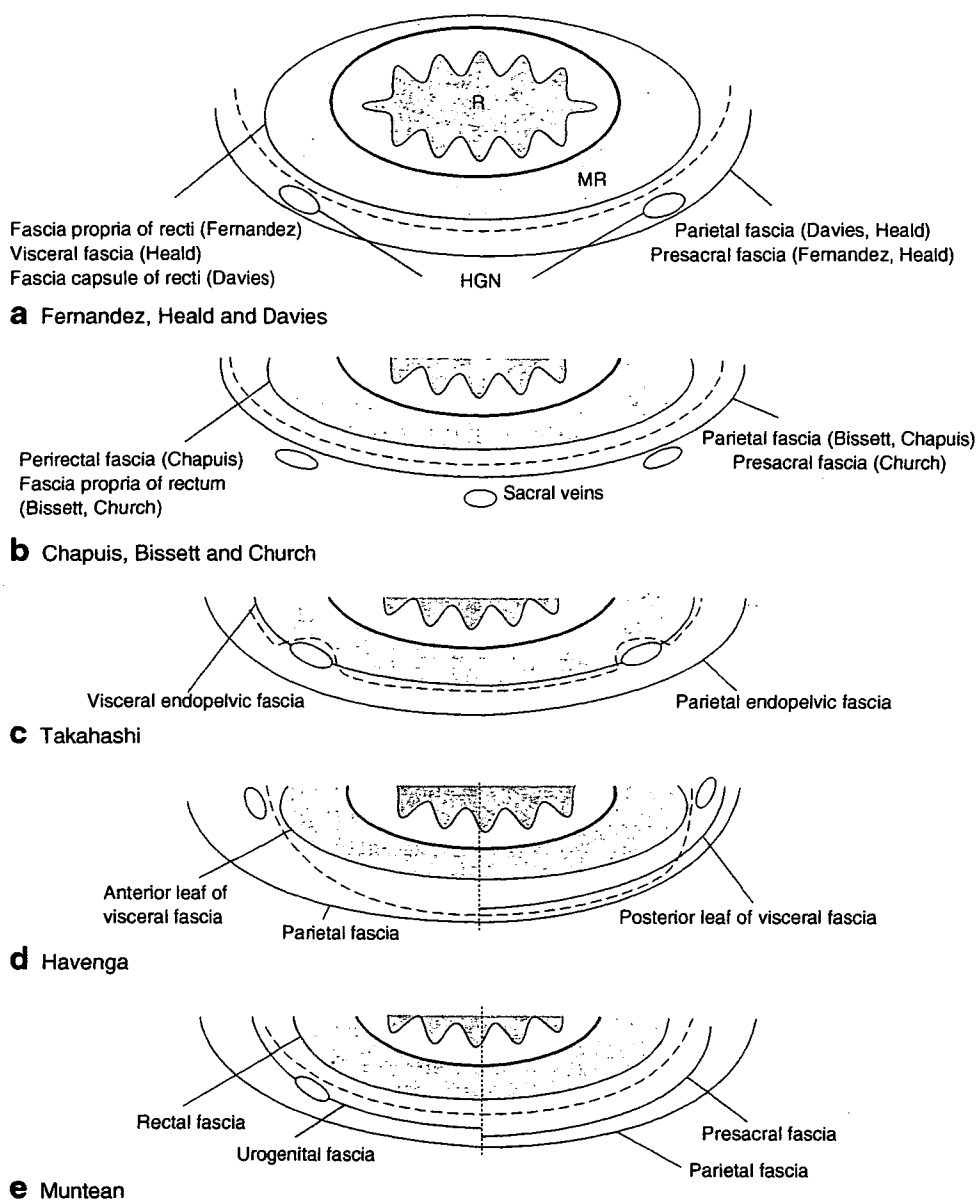
A comprehensive understanding of the fascial structures posterolateral to the rectum is critically important to rectal surgeons. To avoid presacral venous bleeding, autonomic nerve injury and local recurrence, posterior and lateral mobilizations of the rectum are performed according to the fascial structures<sup>1-5</sup>. However, descriptions of these fasciae differ in certain critical aspects, although there is consensus that the mesorectum is surrounded by visceral fascia<sup>6</sup> or the fascia propria of the rectum (FPR)<sup>7</sup>. This surrounding fascia has been termed the FPR in the present study. There is controversy about which fascia covers the hypogastric nerve (HGN) (*Fig. 1*) and whether the rectosacral fascia is a real structure<sup>14-17</sup> or a surgical artifact resulting from fascial adhesion<sup>11,18</sup>.

In line with the suggestion of Bissett and Hill<sup>11</sup>, the authors hypothesized that a multilaminar fascial structure seems to have provided different interpretations of the

reliable surgical plane in rectal surgery. As it is possible that pelvic fascial structures are easily created as artefacts in dissection and surgery<sup>19</sup>, a comprehensive histological study using large sections covering wide areas around the mesorectum is needed. The authors recently demonstrated histologically that one of the lateral continuations of Denonvilliers' fascia separates the HGN and pelvic plexus from the mesorectum<sup>20</sup>. One of the aims of the present study was therefore to examine whether Denonvilliers' fascia continues and connects to one of the retrorectal fasciae.

## Methods

Pelvic visceral materials for histological assessment were obtained from 12 male cadavers that had been donated to Sapporo Medical University. Mean age at the time of death was 82.4 (range 71-95) years. Ten cadavers had been fixed by arterial injection of 10 per cent formalin solution.



**Fig. 1** Previous interpretations of retrorectal fascial structures by **a** Fernandez-Represa *et al.*<sup>8</sup>, Heald and Moran<sup>6</sup> and Davies<sup>9</sup>, **b** Chapuis *et al.*<sup>10</sup>, Bissett and Hill<sup>11</sup> and Church *et al.*<sup>12</sup>, **c** Takahashi *et al.*<sup>13</sup>, **d** Havenga *et al.*<sup>14</sup> and **e** Muntean<sup>15</sup>. In **d** and **e** the superior level is shown on the right and the inferior level on the left. The surgical plane is shown as a dashed line. HGN, hypogastric nerve; MR, mesorectum, R, rectum

For fresh cadaver dissection under complete bacterial control, two frozen pelvises were immersed and thawed overnight in physiological saline containing 0.1 per cent sodium azide. Surgical dissection of the rectum was performed by two experienced colorectal surgeons. These specimens were embedded in paraffin, then semiserial horizontal sections (10–20 µm thick) were prepared between the levels of the first and fifth sacral vertebrae

at 1.0–2.0-mm intervals, and stained using haematoxylin and eosin. Sagittal sections (20 µm thick) were made at the midline of sacral vertebrae. Levels caudal to the fifth sacral vertebra were not examined. Combined observations of horizontal and sagittal sections, especially both types of section from the same specimen, provided detailed information about whether a fascia was continuous or interrupted.