hospital in a hurry. Obviously, this situation in Japan is wasting medical funds. It goes without saying that the situation must be improved.

The mean operative time in the current study was a little longer than in previously reported studies. This may be attributable to the fact that at our institution, trainee doctors perform part or all of a surgical procedure under the guidance of staff doctors in many cases. Also, we are unable to make a laparoscopic team. However, it is evident from results of this study that the quality of our operations has not been lowered.

In conclusion, the current study demonstrates that Lap-LAR can be performed safely without increased morbidity or mortality, and that it offers benefits in terms of faster recovery of bowel motility and shorter hospital stay comparable with patients who undergo Lap-colectomy. With improvements in technology and surgeons' experience, we believe that the use of this procedure will expand. Analysis of long-term oncologic outcomes for patients with colon and upper rectal carcinoma will take place in a few years time. It remains unclear, however, whether laparoscopic resection for middle and lower rectal carcinoma is equivalent to conventional open surgery in terms of oncologic outcome, and this can determined only by evaluation of multiple randomized studies.

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Diseases of the Colon & Rectum

# Total Pelvic Exenteration With Distal Sacrectomy for Fixed Recurrent Rectal Cancer in the Pelvis

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PURPOSE: This study evaluates the effectiveness of total pelvic exenteration with distal sacrectomy for fixed recurrent tumor that developed from primary rectal cancer. METHODS: We investigated surgical indications, techniques to minimize blood loss and reduce complications, and oncological outcomes in 57 patients who underwent total pelvic exenteration with distal sacrectomy between 1983 and 2001. RESULTS: Forty-eight patients (84 percent) had negative margins. A comparison between two periods (1983-1992 and 1993-2001) showed that mean blood loss decreased from 4,229 to 2,500 ml ($P$ = 0.002), indicating a favorable learning curve in minimizing blood loss. Two hospital deaths were observed in the earlier period and none in the later period. The most common sacral amputation level was the S3 superior margin, followed by the S4 inferior margin and the S2 inferior margin. The most frequent complication was sacral wound dehiscence in 51 percent, followed by pelvic sepsis in 39 percent. The incidence of pelvic sepsis in the later period was significantly decreased to 23 percent, compared with 72 percent in the earlier period ($P$ = 0.046). Multivariate analysis showed that negative margins and negative carcinoembryonic antigen predicted improved survival. In 48 patients with negative margins, three-year and five-year disease-specific survival rates were 62 percent and 42 percent, respectively. CONCLUSION: Strict patient selection makes total pelvic exenteration with distal sacrectomy a feasible radical approach for fixed recurrent tumor. Careful performance of this surgical procedure along with the proper steps to decrease blood loss should achieve a favorable learning curve and low rate of surgical complications. [Key words: Rectal carcinoma; Local recurrence; Total pelvic exenteration; Sacrectomy; Surgical resection]

Among recurrent rectal cancers after curative resection, locally recurrent tumor (LRT) is very common. Surgical series have shown that isolated LRT occurs in 4 percent to 33 percent of patients after curative resection, but effective treatment remains to be established.[1,2] For LRT cases, forms of radiotherapy, such as external beam radiotherapy and intraoperative radiotherapy (IORT), chemotherapy, and surgical treatment have been employed singly or as part of multimodality treatment over the last several decades. Such treatment has resulted in certain outcomes but none that are completely satisfactory.[3–13]

With the aid of high-quality tumor-site imaging studies, we have determined that radical resection with removal of affected neighboring structures was the only curative approach for LRT, as originally reported by Wanebo and Marcove.[3] In this study, we describe the surgical indications, technical aspects, and oncologic outcomes of total pelvic exenteration with distal sacrectomy (TPES) for fixed recurrent tumor (FRT).

## PATIENTS AND METHODS

We investigated a total of 163 consecutive patients undergoing laparotomy to remove LRT between 1983

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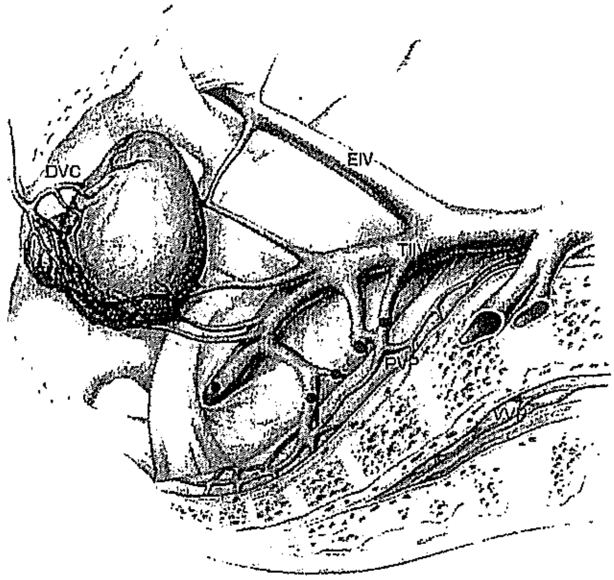
**Table 1.**
Patient Characteristics (N = 57)

| | |
|---|---|
| Median age in years (range) | 55 (29–73) |
| Gender | |
| Male | 44 |
| Female | 13 |
| Body mass index (range) | 22.8 (15.0–28.7) |
| Median time (months) to local recurrence (range) | 23 (7–102) |
| Liver metastasis | |
| No | 52 |
| Yes | 5 |
| Initial surgery | |
| Sphincter-preserving surgery | 28 |
| Abdominoperineal resection | 29 |
| Radiotherapy for primary rectal cancer | |
| Yes | 2 |
| No | 55 |
| Radiotherapy for local recurrence before re-resection | |
| Yes | 23 (median,50 Gy; range, 30–80 Gy) |
| No | 34 |
| Dukes classification for primary growth | |
| A | 3 |
| B | 16 |
| C | 38 |
| Histologic type | |
| Well-differentiated adenocarcinoma | 22 |
| Moderately differentiated | 27 |
| Poorly differentiated | 8 |




DVC: dorsal vein complex
EIV : external iliac vein
TIIV : trunk of internal iliac vein
BIIV : branch of internal iliac vein ●
PVP : presacral venous plexus
VVP : vertebral venous plexus

**Figure 1.** Intrapelvic venous plexus. DVC = dorsal vein complex; EIV = external iliac vein; PVP = presacral venous plexus; TIIV = trunk of internal iliac vein; VVP = vertebral venous plexus.

and 2001. The study excluded patients whose recurrent rectal cancer developed after local excision. In all patients, computed tomography of the lung, liver, and pelvis was performed, and serum carcinoembryonic antigen (CEA) was measured. After 1988, we employed magnetic resonance imaging. Positron emission tomography was not available during this period. We performed abdominoperineal resection or other limited surgeries in 51 patients, total pelvic exenteration (TPE) in 38 patients, and TPES for FRT in 55. The remaining 19 had unresectable LRT. Two patients receiving abdominoperineal resection with sacrectomy were included in the group of patients undergoing TPES for later analyses. Of the 57 TPES patients, 5 had their initial surgery at our institution, and the other 52 had it done at another institution. This study was designed to evaluate the significance of TPES for FRT. Patient characteristics are listed in Table 1. Median follow-up for survivors was 42 (range, 17–163) months. Disease-free survival (DFS) and disease-specific survival (DSS) curves were calculated with the Kaplan-Meier method. Multivariate Cox regression and log-rank test were used to compare survival curves. The difference between crude proportions was assessed by means of the chi-squared method.

## Techniques to Reduce Surgical Invasiveness

*Measures Against Blood Loss from Intrapelvic Venous Plexus (IVP).* A schematic of the IVPs we encounter is shown in Figure 1. We had no methodical strategy for dealing with IVPs until 1992, but have devised the following procedure for dissecting IVPs on the basis of reviews of previous TPES surgeries to reduce blood loss. First, the dissection is made toward the distal sacrum while concurrently resecting the thickened Waldeyer's fascia with the presacral venous plexuses. Bleeding from this venous plexus can be stopped through a combination of electric cautery and gauze pack hemostasis. The important point in prevention of bleeding is the order in which ligations

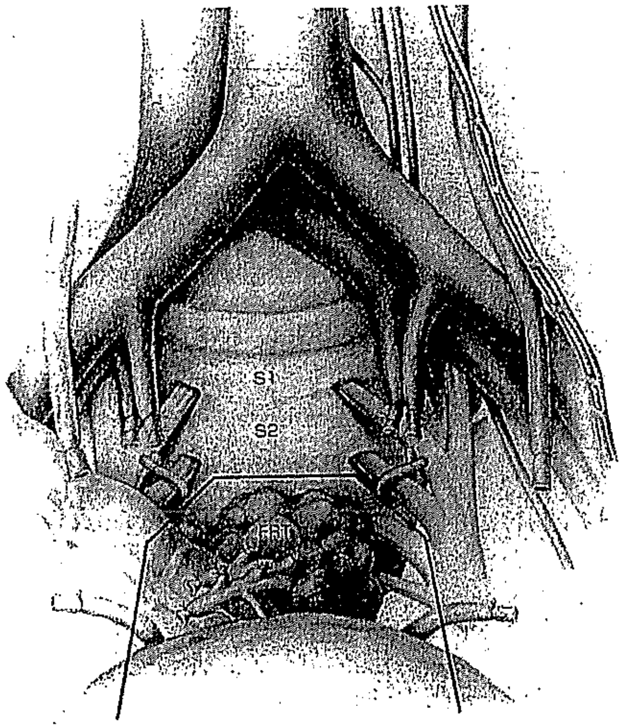



**Figure 2.** Schema of sacrectomy line and marked second sacral nerve. FRT = fixed recurrent tumor.

are done for two veins: 1) the dorsal penile complex and 2) the trunk of internal iliac vein (TIIV). The dorsal penile complex should be cut before the ligature of the TIIV. In treating the internal iliac vessels (both artery and vein), first the arterial trunk is doubly ligated and divided bilaterally, and then several branches of the internal iliac vessels perforating the pelvic wall are divided. Finally, the TIIV is tied and divided. Then, the patient is placed in a prone position for sacrectomy, using the padding operating frame to avoid increasing abdominal and vertebral venous pressure. To reduce bleeding during sacrectomy, detachment of the sacrospinous and sacrotuberous ligaments and muscles before sacral amputation is essential. Resection of the internal iliac vessels can greatly contribute to reducing blood loss during sacrectomy.

*Avoidance of Sacral Nerve Injury.* We perform sacral amputation at or below the inferior margin of the second sacrum so that better postoperative quality of life (QOL) might be attained. Lumbosacral, and S1 and S2 sacral nerves can be identified during resection of the internal iliac vessels. The S2 sacral nerve can be marked with a rubber loop (Fig. 2) during the abdominal phase so that misrecognition of sacral nerves is prevented during sacrectomy.

## RESULTS

Microscopically negative margins (R0) were seen in 48 patients (84 percent) and positive margins were seen in 9 patients; 3 of these patients received IORT in a palliative setting. A comparison between two periods (1983–1992 and 1993–2001) showed that mean blood loss decreased from 4,229 to 2,500 ml ($P$ = 0.00207), indicating a favorable learning curve in minimizing blood loss (Table 2). There was no difference in operative time and hospital stay. The most common level of sacral amputation was the S3 superior margin in 23 cases, followed by the S4 inferior margin and the S2 inferior margin (Table 3). Three patients had more than 10 liters of blood loss, but all of them underwent TPES during the earlier period. Among them, there were two hospital deaths caused by renal failure and sepsis because of serious pelvic infection, respectively. No hospital death occurred in the latter period. The overall complication rate was 58 percent. The most frequent complication was sacral wound dehiscence in 51 percent, followed by pelvic sepsis in 39 percent. The incidence of pelvic sepsis in the later period was significantly decreased to 23 percent, compared with 72 percent in the earlier period ($P$ = 0.046). Enteroperineal fistula (as caused by pelvic sepsis) was observed in three patients and as a late complication after radiotherapy in one; all the four patients underwent bypass surgery. One patient receiving 50 Gy radiotherapy had ileal conduit breakdown four months after TPES and needed bilateral nephrostomy for urine control. He has survived for more than nine years with impaired QOL. There was no correlation between level of sacrectomy and complications. All patients had denervation pain around the buttock lasting two to six months after TPES. Two patients needed analgesic drugs for more than one year and had no local re-recurrence.

Multivariate analysis of the eight factors shown in Table 4 indicates that R0 resection and negative CEA predicted improved survival. Survival curves show overall three-year DSS, DFS, and local control rates of 54 percent, 48 percent, and 57 percent, respectively, and overall five-year rates of 36 percent, 31 percent, and 41 percent, respectively. In 48 patients with R0, including five cases of hepatic metastasis, the three-year and five-year DSS rates were 62 percent and 42 percent, respectively, whereas there was no four-year survivor in those with R-positive, a result showing a significantly poor prognosis ($P$ = 0.00778) (Fig. 3). There was no survival difference between those with

**Table 2.**
Surgical Invasiveness and Hospital Stay

| | Earlier Period (1983–1992) (n = 18) Mean (Range) | Latter Period (1993–2001) (n = 39) Mean (Range) | *P* Value |
|---|---|---|---|
| Operative time (minutes) | 769 (370–990) | 682 (480–1,100) | 0.38992 |
| Blood loss (ml) | 4,229 (1,800–16,300) | 2,500 (673–8,468) | 0.00207 |
| Hospital stay (days) | 37.5 (23–200) | 35 (21–257) | 0.2216 |

**Table 3.**
Level of Distal Sacrectomy and Complications

| | Sepsis in Pelvis | Ileus | Fistula[a] |
|---|---|---|---|
| Middle amputation | | | |
| S2 inferior margin (n = 9) | 5 | 2 | 1 |
| S3 superior margin (n = 23) | 8 | 1 | 1 |
| Low amputation | | | |
| S3 inferior margin (n = 10) | 5 | 1 | 2 |
| S4 superior margin (n = 10) | 2 | 1 | |
| S4 inferior margin (n = 5) | 2 | | |

[a]Intestinal-perineal fistula caused by anastomotic leakage.

and those without radiotherapy before re-resection. Of five patients with synchronous hepatic metastasis, three were alive without signs of re-recurrence at 13, 26, and 96 months, respectively. Thirteen patients (23 percent) had lateral node metastases. Of these, six are alive, and three were long-term survivors for 64, 68, and 123 months, respectively. The most common site of re-recurrence was lung in 13 patients, followed by pelvis in 12.

## DISCUSSION

If a patient with LRT has intractable pain, perineal ulcer, or other comorbid conditions, the QOL deteriorates remarkably, and probably has a miserable prognosis. Nevertheless, studies show that one-half of recurrences are confined to the pelvis without distant metastasis.[1]

Wong *et al.* evaluated the effect of radiotherapy on LRT, indicating that radiotherapy did not contribute to survival benefit as seen in other reports.[4,9] Attempts to improve outcomes by combining resection and IORT have been well described.[7,8,10,11] In fact, therapeutic policies for LRT vary remarkably. This is probably because 1) there are a variety of LRTs, ranging from mobile anastomotic recurrence to a huge mass occupying the pelvis; 2) an inappropriate surgical intervention may cause an iatrogenic cancer spread, leading to impaired QOL; and 3) although treatments other than complete resection may not produce a cure, the invasiveness of extended surgery is considered excessive.[10,11] If LRT involves only anterior organs, partial or total removal of the involved organs can achieve adequate surgical margins. A challenge is how to perform surgical treatment for FRT involving dorsal and/or dorsolateral structures, which accounts for a larger percentage of LRTs. In case of FRT, fixation is infrequently confined to one site and of a small range. In addition, anatomic planes in the pelvis are distorted by the initial surgery and it is difficult to determine and hold uninvolved margins during resection, especially after radiotherapy. For FRT, therefore, composite resection is inevitably required to encompass potentially involved pelvic walls. Wanebo tackled this problem with a new technique called abdominosacral resection, which was used by several other surgeons in the 1980s.[3,6,14,15] An FRT extends along the internal iliac vessels more frequently than primary rectal cancer, hence bilateral resection of internal iliac vessels is one of the pivotal steps in TPES.[16] The improved method of dealing with the intrapelvic venous system has allowed us to complete TPES with decreased blood loss, resulting in a favorable learning curve with low morbidity and no hospital deaths in the latter period. TPES has nonetheless been generally thought to be a demanding and formidable technique, consequently, the combination of limited resection and IORT is likely to become a standard procedure in the treatment for LRT.[5,7,8,10,11] Shoup *et al.* reported improved survival with resection and IORT, and a five-year DSS rate of 51 percent. However, their results cannot be easily compared with our results from treating FRTs, because they studied various LRTs.[13]

With regard to surgical indication, we performed TPES for FRT localized in the pelvis without distant metastasis. In cases of distant metastasis, however, we extended the indications to single-liver or two-liver metastases, but excluded lung metastasis and other

Table 4.
Clinicopathologic Variables and Survival Analysis

| Variable (n) | Univariate Analysis 5-Year Survival (%) | Univariate Analysis P Value | Multivariate Analysis Relative Risk | Multivariate Analysis P Value |
|---|---|---|---|---|
| Surgical margin | | | | |
| Negative (48) *vs.* positive (9) | 42 *vs.* 0 | 0.0012 | 3.39 | 0.0045 |
| Serum CEA level | | | | |
| <5 (18) *vs.* >5 (39) | 54 *vs.* 26 | 0.0287 | 2.76 | 0.0257 |
| Range of pain | | | | |
| Limited (32) *vs.* radiating to buttock or thigh (25) | 46 *vs.* 21 | 0.0431 | | |
| Tumor size, <5 cm (25) *vs.* >5 cm (32) | 32 *vs.* 39 | 0.9115 | | |
| Level of sacrectomy, middle (32) *vs.* low (25) | 36 *vs.* 36 | 0.9345 | | |
| Bone invasion, negative (45) *vs.* positive (12) | 35 *vs.* 39 | 0.9731 | | |
| Type of initial operation | | | | |
| Abdominoperineal (29) *vs.* low anterior (28) | 30 *vs.* 42 | 0.3213 | | |
| Lateral node metastasis | | | | |
| Negative (44) *vs.* positive (13) | 42 *vs.* 34 | 0.9661 | | |

CEA = carcinoembryonic antigen.

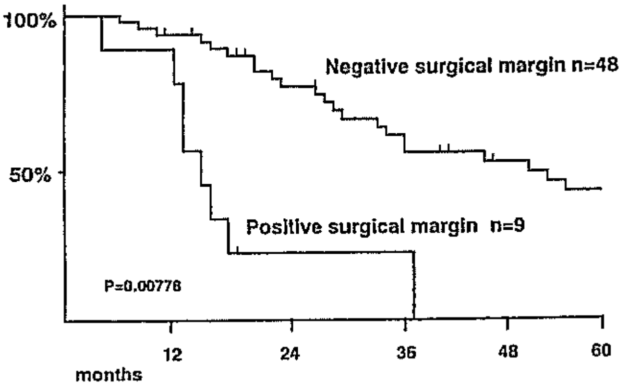



**Figure 3.** Disease-specific survival curve. The difference between the two groups was significant ($P < 0.00778$).

extrapelvic diseases. Contraindications included unresectable locally recurrent tumors growing into the sciatic notch, encasing the external iliac vessels, extending to the sacral promontory, or having leg edema from lymphatic and/or venous obstruction.

If prevention of pelvic infection is maintained, TPES can be a more acceptable and stable procedure for the treatment of LRT. Important factors in using TREP are prevention of bacterial contamination and complete hemostasis. Although omentoplasty into the pelvic cavity should be performed in all patients who have sufficient omentum, it was performed in only 60 percent of our patients in the latter period. Mannaerts *et al.* reported favorable results from using methods of filling dead space such as the musculocutaneous flap. They suggest that if omentoplasty cannot be performed, the musculocutaneous flap or the Vicryl mesh should be aggressively used.[11] We constructed ileal conduit in all patients. Ileoileostomy, after ileal conduit is constructed, should be lifted up above the pelvic brim and fixed to the mesentery so that it will not fall in the pelvis. This procedure is invariably required to prevent anastomotic leakage caused by pelvic sepsis, especially after radiotherapy.

Since we adopted the policy of preserving the bilateral S2 sacral nerves, serious complications such as walking disorder and spinal fluid leak have not occurred. In an outpatient clinical setting, we interviewed all 12 patients without re-recurrence who survived more than three years about their QOL. Although a decline in QOL caused by the double stomas is inevitable, they were able to return to work with satisfaction.[17]

Several factors, such as type of initial surgery, tumor size, and presence of severe symptoms, have been regarded as significant prognostic indicators, although a consensus on this has not been reached. It has previously been shown that in surgical treatment of primary rectal cancer, surgery-related factors and biologic factors are crucial.[18] The surgeon's technical skills and attitude may have more influence on important factors, including surgical margin status and complications, in LRT surgery than in primary rectal cancer surgery. Extended surgeries such as TPES should thus be undertaken in specialized centers that have an experienced complex-treatment team.

Suzuki *et al.* have established the degree of fixation to surrounding structures according to surgical and pathologic findings and have proposed their own staging method.[8] A staging system should be determined according to the degree of fixation and/or other prognostic factors so that treatment modalities for LRT, especially surgical treatment, are given their appropriate place.

TPES has not been widely employed. However, with strict patient selection, TPES can be a feasible radical approach for FRT. Careful performance of TPES along with the proper steps to decrease blood loss from IVP should achieve favorable results. TPES can thus be included in the group of techniques that are stable and have fewer complications.

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## Invited Commentary

To the Editor—Despite improvements in adjuvant therapy regimens and the virtually universal adoption of total mesorectal excision (TME) for surgical resection of middle and lower third rectal cancers, pelvic recurrence of rectal cancer remains a challenging clinical problem. Many of these patients have truly isolated locoregional recurrence and die with poorly controlled pelvic pain. External beam radiotherapy (EBRT) provides transient palliation but does not offer the hope of long-term survival.[1] Surgical resection of recurrent rectal cancer, particularly with involvement of the sacrum, is a formidable undertaking but offers three-year survival as high as 40 percent and five-year survival of 15 percent to 30 percent.[2–4]

Dr. Moriya and colleagues have presented a series of 57 patients who underwent total pelvic exenteration–distal sacrectomy (TPES), also known as abdominosacral resection (ASR), for resection of fixed pelvic recurrence of rectal cancer. In their total series of 163 patients with recurrent rectal cancer, 51 patients (31 percent) had disease amenable to resection by abdominoperineal resection, 38 (23 percent) by total pelvic exenteration, and 55 (34 percent) by TPES; 19 patients (12 percent) had unresectable recurrence. It is important to note that fully one-third of the patients with pelvic recurrence of rectal cancer required TPES to achieve complete resection.

Multiple studies have shown that the most important prognostic factor in patients with recurrent rectal cancer is the ability to achieve complete resection. The authors report an admirable R0 resection rate of 84 percent, with an overall mortality of 5.3 percent (3 of 57 patients). Median follow-up for survivors was 42 months. Disease-specific survival for the patients who had R0 resection was 62 percent at three years and 42 percent at five years; this is an excellent result in this challenging group of patients. The most frequent complications were wound dehiscence (51 percent) and pelvic sepsis (39 percent). A multivariate analysis confirmed the presence of a negative surgical margin and CEA level <5 ng/ml as significant prognostic factors.

It is of interest in this series that only two patients (3.5 percent) had radiation for their primary rectal cancer, and less than one-half of the patients (23 patients, or 40.4 percent) had radiation before resection of their local recurrence. This represents a significant variance from American series. In most Western countries, radiation has become standard for adjuvant treatment of high-stage (Stage III or IV) primary rectal cancer. In our own experience, almost all patients with recurrent rectal cancer have received adjuvant radiation as part of their treatment for primary rectal cancer; of those patients who did not receive adjuvant radiation for the primary tumor, all without exception had radiation once recurrence was documented.

This highlights the issue regarding the most appropriate primary treatment for prevention of recurrence of rectal cancer. The adoption of total mesorectal excision (TME), championed by Heald *et al.*,[5] has revolutionized the surgical management of primary rectal cancer. This remarkable surgical achievement, which is a simple refinement of a very old technique, has greatly altered the oncologic landscape and permitted high local control rates with surgery alone. However, these results can be complemented by radiation, as underscored by the Dutch study.[6] The combination of excellent surgical control through R0 resection by the TME technique coupled with appropriate adjuvant radiation and chemotherapy in high-risk patients can greatly enhance the outcome in rectal cancer treatment, and diminish the need for retrieval surgery.

These comments notwithstanding, the technique reported here by Dr. Moriya and colleagues complements many other series and highlights the need to maintain techniques for control of local recurrence when it does occur. In our own series of patients with pelvic recurrence of rectal cancer, the majority had previously received adjuvant radiation. All had been resected by experienced surgeons, and many came to us to undergo "salvage" surgery after previous attempts had failed. In this challenging group of patients, we were able to achieve wide-field abdominosacral resection with no remaining disease in approximately 85 percent of patients, with five-year overall survival of 30 percent. These results are obtained at a cost, however; overall mortality in our series was 6 percent, and overall morbidity was substantial (in keeping with all other series, including the present report). Our ultimate goal should be the elimination of local recurrence of rectal cancer, so that aggressive resection techniques become unnecessary.

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## The Authors Reply

To the Editor—We are grateful for Professor Wanebo's and Dr. Varker's various thoughtful comments on our study. We read the Wanebo and Marcove article of 1981, and experienced our first case of total pelvic exenteration–distal sacrectomy (TPES) in 1983. As of March 2004, we have performed TPES in 74 cases. One of the factors that complicate this surgery is the dense scar made after radiotherapy or D3 dissection including lateral node dissection. As accurately commented, in cases that undergo surgery after radiotherapy (previously irradiated cases), the appropriate dissection layer is distorted by the scar tissue, and thus the surgery tends to become excessively invasive. Radiotherapy has been used in less than one-half of our cases, but in Western countries, almost all of the cases are previously irradiated individuals. In this regard, our series is weighted in favor of surgery. In addition, Japanese patients have lower rates of obesity, atherosclerosis, and cardiovascular diseases that predispose toward complications, and we believe these factors have enabled us in obtaining a good learning curve. Also, when extended surgery is performed as the initial surgery, there is a chance of encountering greater difficulty in dissection than after radiotherapy, because of the postoperative scarring. Such cases cause Japanese surgeons considerably more stress than do irradiated cases. The difference in therapy for primary rectal cancer between Western countries and Japan (total mesorectal excision + radiotherapy *vs.* nerve-sparing surgery with D3) influences the relative difficulty of surgery for locally recurrent cancer. Probably this is the age of surgical conservatism, but we believe it is necessary to stress that some cases can be expected to be cured only by TPES. Although TPES has become a standard surgical technique, it is a mode of therapy that must be performed on the basis of strict patient selection. If possible, we wish to develop a less invasive surgical procedure that takes the place of TPES, by use of adjuvant therapies such as intraoperative radiotherapy and new antitumor drugs.

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# Total Pelvic Exenteration with Distal Sacrectomy for Fixed Recurrent Rectal Cancer

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Four percent to 33% of patients with rectal cancer develop locoregional relapse after undergoing radical surgery with curative intent. Without treatment, the mean survival time for patients with local recurrence is only approximately 8 months, an associated severe symptomatic disease—especially pain—occurs, and their quality of life becomes remarkably deteriorated, probably with a miserable prognosis [1–4].

For cases with locally recurrent rectal cancer (LRRC), external beam radiotherapy, intraoperative radiotherapy, chemotherapies, and surgical treatments have been used singly or as part of a multimodality approach over the last several decades, resulting in certain outcomes that are not yet satisfactory [5–21]. For the purpose of attaining thorough margin-free resection, what we have been performing actively as our standard curative approach for fixed recurrent tumor (FRT) is radical resection with removal of affected neighboring organs and pelvic walls, including the sacrum, as originally reported by Wanebo and Marcove [6]. This article describes the surgical indications, contraindications, surgical techniques, oncologic outcomes, and complications of total pelvic exenteration with distal sacrectomy (TPES).

## Patterns of growth in the pelvis

By cause and growth pattern of local recurrence, LRRC can be classified into three main categories.

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*Anastomotic recurrence and perianastomotic recurrence*

These suture line recurrences after low anterior resection are caused by implantation of cancer cells into the stump of anastomosis or insufficient resection of the rectal wall or mesorectum (Fig. 1). In the case of extramural invasion, however, it is difficult to distinguish between these two recurrences. When there is no extramural invasion or neighboring organ invasion, the basic surgical procedure is abdominoperineal resection (APR).

*Perineal recurrence*

Perineal recurrence is a recurrence that occurs after APR near the pelvic floor or perineal wound. From its early stage, perineal recurrence invades the coccyx, gluteal maximus muscle, or pelvic wall. Surgical margin-free resection seldom can be obtained by local excision alone. Many patients need resection of the pelvic wall or intrapelvic organs.

*Pelvic recurrence*

By occupied site, pelvic recurrence (Fig. 2) can be subdivided into anterior, lateral, and dorsal recurrences. Anterior pelvic recurrence is an LRRC that invades the anterior organs (ie, urogenital organs). For resecting this recurrent tumor, the basic surgical procedure is total pelvic exenteration (TPE). In women, if there is no obvious bladder invasion, it is possible to preserve urinary organs. This recurrence frequently is caused by insufficient resection for T4 rectal cancer. Lateral pelvic recurrence occurs because of lateral lymph node metastasis after total mesorectal excision or insufficient lateral node dissection. It begins to infiltrate the pelvic wall in its early stage. Dorsal pelvic recurrence is presacral extramural recurrence after APR or low

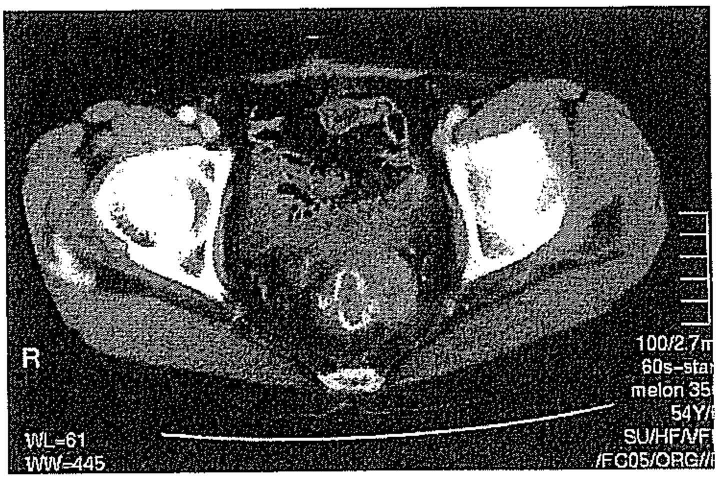


Fig. 1. Perianastomotic recurrence. A 54-year-old female patient underwent TPES for her FRT with 556 mL blood loss and no complication. At initial surgery 4 years ago, she received low anterior resection with D3 lymph node dissection and postoperative 60 Gy radiotherapy.

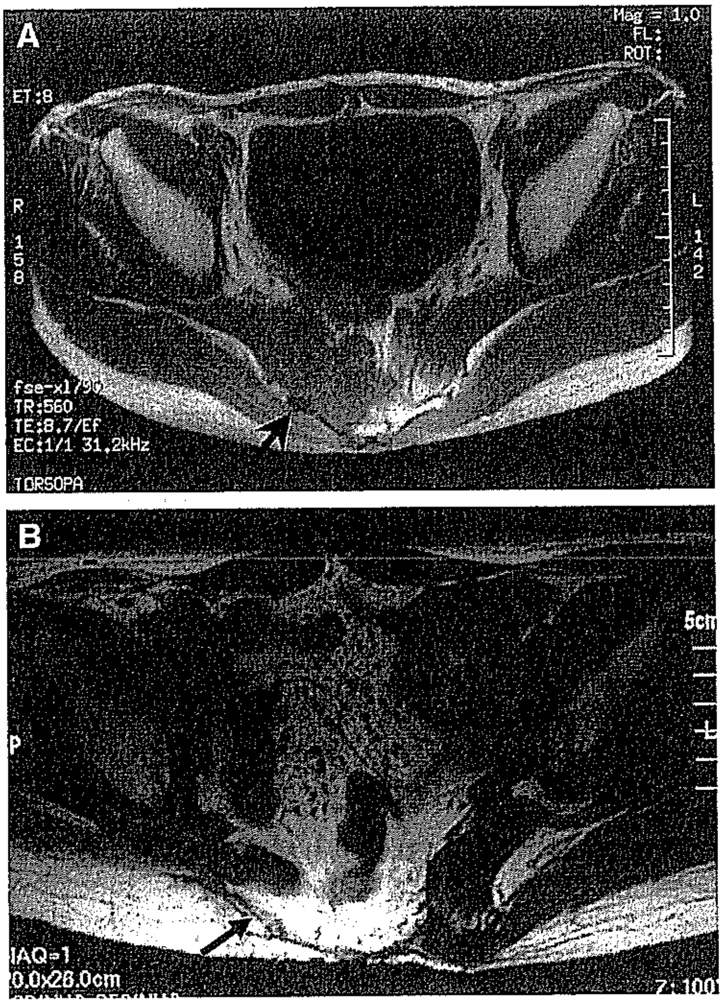


Fig. 2. (*A*) Dorsolateral pelvic recurrence with sacral bone invasion. A 47-year-old male patient underwent TPES for his FRT (*arrow*) with 673 mL blood loss and no complication. At initial surgery 1.5 years ago, he received low anterior resection. (*B*) Postoperative MRI. The patient is alive without re-recurrence 4 years after TPES.

anterior resection that invades the pelvic wall. It forms itself into FRT from its early stage. The cause of this recurrence may be extramesenteric lymphatic spread, insufficient resection of the mesorectum, or a cut into the mesorectum during operation. This pattern of recurrence is common patterns.

## Why total pelvic exenteration with distal sacrectomy is the standard surgery for fixed recurrent tumor

Therapeutic policies for LRRC vary remarkably. The probable reasons for this are as follows: (1) there are various LRRCs, ranging from mobile recurrences to huge masses that occupy the pelvis, (2) an inappropriate surgical intervention may cause an iatrogenic cancer spread, leading to impaired quality of life, and (3) although treatments other than complete resection may not bring cure, the invasiveness of surgeries such as TPES is considered excessive. In non-fixed recurrent tumors, complete resection can be achieved more often with limited surgery, such as APR or low anterior resection, and the outcomes are relatively favorable. LRRC grows within the narrow pelvis, and when the tumor size becomes larger to some extent, it can invade the pelvic wall easily and appear in the form of FRT. A challenge for the surgeon is the surgical treatment for FRTs with lateral or dorsal involvement, which comprises a larger percentage.

Such fixation is infrequently confined to one site and is of small range; many of those cases show fixations to the components surrounding the LRRC (eg, bony pelvis, including sacrum and coccyges; non-bony pelvis, including coccygeus muscle, piriform muscle, internal iliac vessels, inferior hypogastric plexus, sacral nerve plexus, obturator internus muscle, and sacrospinous and sacrotuberous ligaments; and residual anterior organs in the pelvis). Their anatomic planes are distorted, and it is difficult to determine and hold uninvolved margins during resection. For FRT cases, composite resection is inevitably required to encompass potentially involved pelvic walls, especially the distal sacrum. Only this strategy enables the R0 extirpation en bloc. Especially after APR, the LRRC grows while being sandwiched between the anterior organs and sacrum. Wanebo and Marcove [6] tackled this difficult problem using the new technique of abdominosacral resection, followed by several surgeons in 1980s [8,9,10,12].

Techniques to preserve the anterior organs and inferior hypogastric plexus for surgical treatment of FRT have been reported [16]. Those approaches, however, are likely to reduce local radicality, because the anatomic pathway around the autonomic nerve plexuses and ureter disappears and is replaced by scar tissue caused by initial surgery, especially after extended surgery. FRT in the deep pelvis also is often fixed more extensively than expected before surgery, which also justifies our experience-based strategy that TPES is positioned as the standard surgery for FRT. This technique is considered to be demanding and formidable because of high rates of mortality and morbidity [6,12,13,19]; consequently, combination of limited resection and intraoperative radiotherapy is likely to become standard in the treatment of FRT [17,22–29]. Whether an emphasis is placed on composite resection or multimodality treatment, surgeons have the same view that the key treatment to obtain local control and survival benefit is R0 surgery [22,28–31]. Is it really possible to carry out R0 resection for FRT by conventional surgery? Having been able to ensure R0 resection for FRT and develop secure surgical techniques, we consider that there are no therapies superior to TPES in treating FRT.

## Evaluation by imaging and patient selection

Once the diagnosis of LRRC is made, detailed study should be conducted in terms of surgical indication from two aspects: (1) whether distance metastasis is present and (2) to what extent the tumor spreads within the pelvis. Extrapelvic disease is searched for by the whole body CT scan. MRI and F-18-fluorodeoxy glucose position emission tomography (FDG-PET) are also useful in detecting extrapelvic disease and distinguishing between recurrent disease and scar tissue. CT, MRI, and FDG-PET are useful in distinguishing between solitary and multifocal recurrences in the pelvis and between anterior organ involvement and dorsolateral pelvic wall involvement.

We investigated a total of 196 consecutive patients who underwent laparotomy to remove LRRC between 1983 and 2003. The study excluded patients whose recurrent rectal cancer developed after local excision. We performed a limited surgery, such as APR, in 62 patients, TPE in 41, and TPES in 69. The remaining 24 patients had unresectable LRRC. Clinical and pathologic characteristics of 69 patients are listed in Table 1.

Patients with documented distant metastasis are not candidates for surgical treatment, because the curative potential is low and their life expectancy is not long enough to evaluate treatment outcome. With regard to surgical indication, we conducted TPES for FRT localized in the pelvis. Locally unresectable diseases include tumors that grow into sciatic notch,

Table 1
Clinical and pathologic characteristics of 69 patients

| Characteristics | Number |
|---|---|
| Median age (range) (y) | 57 (29–73) |
| Sex | |
| Male | 55 |
| Female | 14 |
| Body mass index (range) | 22.9 (15.0–28.7) |
| Median time to local recurrence (range) (mo) | 23 (7–118) |
| Liver metastasis | |
| No | 65 |
| Yes | 5 |
| Initial surgery | |
| Sphincter-preserving surgery; SPS | 33 |
| Abdominoperineal resection; APR | 36 |
| Radiotherapy for primary rectal cancer | |
| Yes | 4 |
| No | 65 |
| Radiotherapy for local recurrence before re-resection | |
| Yes | 32 (median, 50 Gy; range, 30–80 Gy) |
| No | 37 |
| Dukes classification for primary growth | |
| A | 4 |
| B | 18 |
| C | 47 |
| Histologic type | |
| Well-differentiated adenocarcinoma | 26 |
| Moderately | 34 |
| Poorly | 9 |

encase the external iliac vessels, extend to the sacral promontory, obstruct the bilateral ureters, and cause leg edema secondary to lymphatic or venous obstruction [30,31]. For patients with one or two liver metastases amenable to surgical resection, however, concomitant hepatectomy with surgical treatment of LRRC may be warranted. Lung metastasis and other extrapelvic diseases are excluded from surgical indications.

## Surgical technique

TPE for primary pelvic malignancy is performed by first dividing loose connective tissues, such as the Retzius, retrorectal, and obturator spaces, and then dissecting along the parietal pelvic fascia. In recurrent cancer cases, however, those spaces disappear and are replaced by dense scar tissue. Because of this condition, TPES for FRT is a challenging procedure. The operation is performed in the following order.

### *Abdominal phase*

The patient is placed in the lithotomy position. After detaching adhesions caused by initial surgery, the surgeon confirms the localization of the recurrent tumor within the pelvis and the absence of extrapelvic diseases and then makes a final decision to proceed to TPES. First, the Retzius space is opened. The endopelvic fascia and pubo-prostatic ligaments can be identified bilaterally and divided using electric cautery to expose the levator ani muscle. The dorsal vein complex together with the divided endopelvic fascia is bunched with the forceps and doubly tied and divided.

Next, the level of sacral amputation is determined. The anterior area from the aortic bifurcation to the sacral promontory is exposed to enter the anterior surface of the sacrum. The dissection is made using electric cautery down to the distal sacrum, at which point sacral amputation is planned, as is resection of the thickened Waldeyer's fascia with the presacral venous plexuses and scar tissue. During this process, bleeding occurs more or less; however, hemostasis can be obtained using combination of electric cautery and gauze pack. The area from the common iliac artery to the bifurcation between the internal and external iliac arteries is exposed. During dissection of the obturator space while preserving the obturator nerve, components of the sacral nerve plexus, such as the lumbosacral nerve and S1 and S2 sacral nerves, can be identified. Marking the S2 sacral nerve with a rubber loop ensures recognition of sacral nerves during sacrectomy (Fig. 3).

The next step is resection of the internal iliac vessels. The way to manipulate the internal iliac vessels is as follows. First, the trunk of the internal iliac artery is doubly tied and divided at the distal portion of the branching of the superior gluteal artery. Second, several branches that perforate the pelvic wall are divided. Finally, the trunk of the internal iliac vein is doubly tied and divided. Blood loss during TPES mostly occurs from

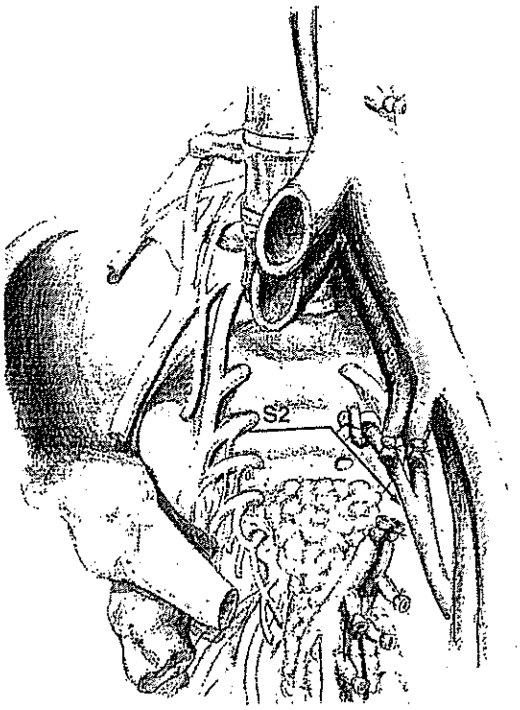


Fig. 3. Line of sacrectomy and marked second sacral nerve.

the venous plexus [31]. By taking the appropriate steps to avoid congestion of the venous plexus at the earliest possible opportunity, the operation can be performed with a minimum amount of blood loss from the venous plexus. Resection of the internal iliac veins is the most important part of this operation, and it requires advanced technical skills and careful maneuvers. FRT extends along the internal iliac vessels more frequently than the primary rectal cancer [32]; bilateral resection of the internal iliac vessels is one of the pivotal steps in TPES. Combined resection of the internal iliac vessels during the abdominal phase greatly contributes to reducing blood loss during sacrectomy.

*Perineal phase*

Incision of the perineal skin conforms to APR. The levator ani muscle is divided at its attachment and a connection is made through to the pelvic cavity. If the perineal phase is performed after the venous plexus is resected, a considerable amount of blood loss will occur from congested veins around the urogenital diaphragm. The perineal phase should occur before ligation of the trunk of the internal iliac veins so that the phase can be performed with less blood loss.

*Sacral phase*

The patient is placed in the prone position after temporary closure of abdominal wound. At that point, the padded operating frame for laminectomy is used to prevent an increase in abdominal or vertebral venous pressure. Bleeding caused by the increase of vertebral venous pressure makes sacral amputation complicated. The median incision is made approximately 10 cm longer toward the head from the planned line of sacral amputation. The gluteus maximus muscle is detached from the sacrum so that the posterior surface of the sacrum can be exposed fully. The next step of this phase involves detaching the sacrotuberous and sacrospinous ligaments and piriform muscle that fix the sacrum. After dissecting these structures, the sacral nerve plexus also can be checked.

The surgeon inserts an index finger into the pelvic cavity from the lower edge of the sacroiliac joint and checks the dissected level of the anterior surface of the sacrum to determine the level of sacral amputation. The medial sacral crest is scraped, laminectomy is performed, and the root of the second sacral nerve is identified. The caudal end of the dura usually extends to around the lower edge of the S2. The dura, together with the cauda equine, is tied and divided. The surgeon performs sacral amputation using chisel and hammer at a stretch (Fig. 4). Hemostasis is performed quickly using electric cautery and bone wax. In men, after checking the stump of the urethra, the urethra is closed tightly to prevent transurethral infection. The origins of the gluteus maximus muscle, the subcutis, and the skin are closed tightly.

*Urinary diversion, prevention of pelvic sepsis, and wound closure*

The patient is placed in the lithotomy position. Reconstruction of the urinary tract using ileal conduit and colostomy is performed. Mobilization of the right colon from the cecum to the hepatic flexure enables construction of a high urostoma. After constructing the ileal conduit, an ileoileostomy

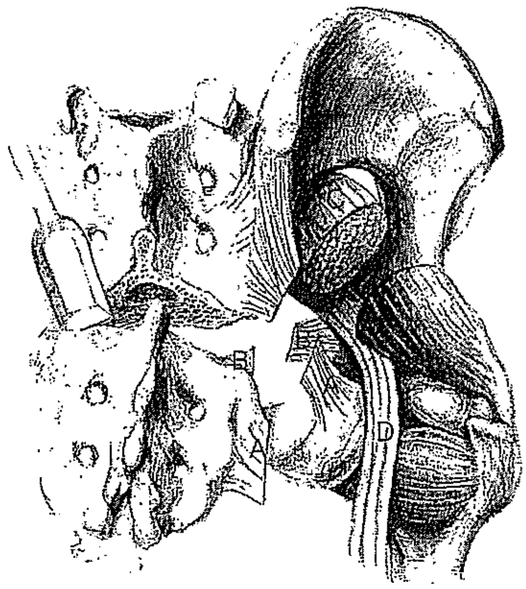


Fig. 4. Sacral amputation in prone position. (*A*) Sacrotuberous ligament. (*B*) Sacrospinous ligament. (*C*) Piriform muscle. (*D*) Sciatic nerve.

should be lifted up above the pelvic brim and fixed to the mesentery so that it will not fall in the pelvic cavity. This procedure is invariably required to prevent anastomotic leakage secondarily caused by pelvic sepsis, especially after radiotherapy. If the greater omentum is long enough with favorable blood flow, omentoplasty into the pelvic cavity should be performed. In patients who have recurrent tumor invading the perineal skin, it is necessary to combine a wide resection of the perineal skin. In such cases, reconstruction should be performed with a musculocutaneous flap [20,30]. It is appropriate that gastrostomy be performed before closing the abdomen, because enteroparalysis continues for a while after TPES. A thick drain is placed in the pelvis, and then the abdomen is closed.

### Surgical invasiveness and oncologic outcomes after total pelvic exenteration with distal sacrectomy

Margins were microscopically negative in 57 patients (83%) and positive in 12. A comparison between two periods (1983–1992 and 1993–2003) showed a mean blood loss decrease from 4229 to 2102 mL ($P < 0.001$), with a favorable learning curve (Table 2). There was no difference in operative time and hospital stay. The most common level of sacral amputation was the S3 superior margin in 26 cases, followed by the S3 inferior margin and S2 inferior margin (Table 3). Overall mortality and complication rates were 3% and 58%, respectively. There was no hospital death in the latter period. The most frequent complication was sacral wound dehiscence in 51%, followed by pelvic sepsis in 39%. The incidence of pelvic sepsis in the latter period decreased significantly to 27%, compared with 72% in the former period ($P = 0.038$). Enteroperineal fistulae were observed in four cases.

Survival curves show overall 3- and 5-year disease-specific survival rates of 58% and 40%, respectively. In 57 patients with R0, including 5 patients with hepatic metastasis, 3- and 5-year disease-specific survival rates were 67% and 49%, respectively, whereas there was no 4-year survivor in patients with margin-positive, which showed significantly poor prognosis ($P < 0.001$) (Fig. 5). There was no survival difference between patients with and without radiotherapy before re-resection. Fourteen patients had lateral node metastases around the internal iliac vessels. Of these 14 patients, 6 are alive and 3 were long-term survivors for 64, 71, and 141 months, respectively.

Table 2
Surgical invasiveness and hospital stay

| Operative burden | Former period (1983–1992) mean $n = 18$ | Latter period (1993–2003) mean $n = 51$ | $P$-value |
|---|---|---|---|
| Operative time (min) | 769 (370–990) | 702 (480–1100) | NS |
| Blood loss (mL) | 4229 (1800–16,300) | 2102 (673–8468) | $P < 0.0001$ |
| Hospital stay (d) | 37.5 (23–200) | 34 (21–257) | NS |

Table 3
Level of distal sacrectomy and complications

| Level of sacrectomy | Sepsis in pelvis | Ileus | Fistula[a] |
|---|---|---|---|
| Middle amputation | | | |
| S2 inferior margin ($n$ = 12) | 6 | 2 | 1 |
| S2-3 ($n$ = 26) | 9 | 1 | 1 |
| Low amputation | | | |
| S3 inferior margin ($n$ = 16) | 8 | 1 | 2 |
| S3-4 ($n$ = 10) | 2 | 1 | |
| S4 inferior margin ($n$ = 5) | 2 | | |

[a] Fistula: enteroperineal fistula caused by anastomotic leakage.

Of 57 patients with R0 resection, 34 developed re-recurrence. The most common site was the lung (18 patients) followed by the pelvis (12 patients).

## Oncologic outcomes reported in the literature

Factors such as type of surgery, combined therapy, and postoperative follow-up period are diversified, and comparison of reported oncologic outcomes for LRRC is of small significance. For example, a study that includes patients with recurrence after local excision naturally should show favorable outcome, whereas in a study conducted only with cases of FRT, unfavorable outcome can be predicted. Lopez-Kostner et al [33] reported a 5-year survival rate of 32% in 43 patients who underwent surgical treatment, 11 of whom developed recurrence after local excision. On the other hand, Bozzetti et al [18] showed a 5-year survival rate of less than 10% in patients who underwent surgery alone and pointed out a limitation of outcome after surgical treatment alone. Regarding 5-year survival after

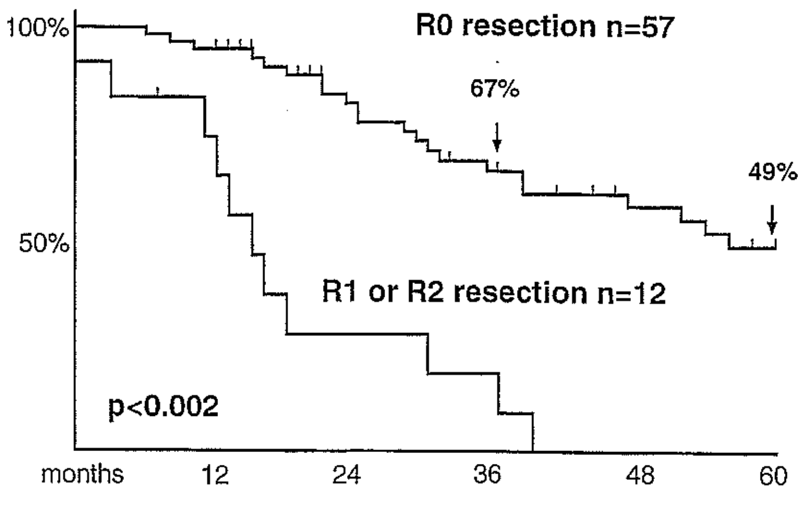


Fig. 5. Disease-specific survival curve. The difference between the two groups was significant ($P < 0.001$).

composite resection, Wanebo et al [19] reported a rate of 31%, Maetani et al [10] reported a rate of 25%, and Yamada et al [21] reported a rate of 18%. Those are not satisfactory outcomes. Incidence of local re-recurrence ranges from 27% to 61% [10,19,31].

As for outcome after multimodality therapy, there are many reports in which the ordinary dosages of radiation used preoperatively were 45 to 50 Gy. Intraoperative dosages of 10 to 15 Gy in R0 cases and 15 to 20 Gy in R-positive cases also were reported [24–29]. Valentini et al [24] reported a 5-year survival rate of 22%, and Mannaerts et al [23] reported a 3-year survival rate of 60%. In the series by Shoup et al [25], who investigated outcomes after resection plus intraoperative radiotherapy, patients with R0 had a median disease-free survival of 31 months and a median disease-specific survival of 66 months.

Lung metastasis and local re-recurrence account for nearly 90% of all re-recurrence patterns [31], and measures to prevent these two types of re-recurrence are important. Compared with 20 years ago, when the only effective antitumor agent was 5-fluorouracil, some effective antitumor agents (eg, CPT-11, UFT, capecitabine, and oxaliplatin) have become available. We think that surgical treatment, combined with composite resection and intraoperative radiotherapy, is indispensable for improving local control rates and that an effective chemotherapy regimen after re-resection is indispensable for inhibiting lung metastasis.

## Prognostic factors and staging system

Several factors, such as type of initial surgery, tumor size, presence of symptoms, and serum carcinoembryomic antigen level, have been regarded as significant prognostic indicators, although a consensus has not been reached yet. Willet et al [11] and Wanebo et al [19] found improved resectability in patients who underwent initial low anterior resection compared with patients who had initial APR. If FRT developed after low anterior resection, however, there was no difference in resectability and survival between them [31]. Shoup et al [25] indicated that vascular invasion and R1/R2 resection are factors for poor prognosis. In either report, the most important factor is whether R0 resection was attained [19,24,25,27,31]. Researchers already have shown that in surgical treatment for primary rectal cancer, surgery-related and biologic factors are crucial [34]. Surgical margin status and complications are exclusively determined by a surgeon's technical skills. Complicated surgeries, such as TPES or abdominosacral resection, should be undertaken only in specialized centers with an experienced complex treatment team.

Suzuki et al [14] judged the degree of fixation to surrounding structures according to surgical and pathologic findings and proposed their own staging method. Valentini et al [24] also reported a similar staging system in