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ORIGINAL CONTRIBUTIONS

Sacropelvic Resection and Intraoperative Electron Irradiation in the Management of Recurrent Anorectal Cancer

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PURPOSE: To provide local control and palliation of pain, a multimodality approach, including external beam radiation therapy, surgical resection, and intraoperative electron irradiation (IOERT), has been used for patients with locally advanced anal or recurrent rectal cancers involving the sacrum. METHODS: Sixteen consecutive patients (11 males; 5 females; ages, 44-76) underwent surgical exploration, sacrectomy, and IOERT, between 1990 and 1994. RESULTS: Proximal extent of resection was S2-3 in four patients, S3-4 in five, and S4-5 in five. Two patients had resection of the anterior table of the sacrum. Margins were clear in 11, close in 3, and microscopically involved in 2 patients. Operative times ranged from 6 to 17 (median, 12.5) hours, and blood loss ranged from 300 to 12,600 (median, 3,350) ml. No operative deaths resulted. Major postoperative complications occurred in eight patients (50 percent): posterior wound infections and dehiscence, urinary leak, and ileal fistula. Five (31 percent) and 3 (19 percent) patients developed no or minor complications, respectively. Intensive Care Unit stay was one night for all patients, and overall hospital stay ranged from 11 to 30 (median, 16.5) days. Follow-up was available on all 16 patients. Kaplan-Meier survival was 68 percent at one year and 48 percent at two years. At the time of analysis, 9 of 16 patients were alive. Of the nine alive patients who responded to a questionnaire, eight reported a reduction in pain and improved quality of life postoperatively. CONCLUSIONS: Sacropelvic resection, in conjunction with IOERT, provides palliation and offers potential for cure in patients with locally advanced or recurrent anorectal cancer. [Key words: Sacropelvic resection; Sacral resection; Rectal cancer; Intraoperative electron irradiation (IOERT); Pelvic recurrence]

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Between 7 and 33 percent of patients with rectal cancer treated for cure will develop isolated locoregional recurrence.[1-9] The fate of patients with locoregional failure is grim, with most at risk for developing disabling complications, including severe pain from nerve involvement and fewer than 5 percent surviving to five years in the absence of surgical intervention.[2, 4, 10] Because autopsy series suggest that 25 to 50 percent of patients with locoregional disease have cancer confined to the pelvis at the time of death,[10, 11] locally aggressive therapies that could palliate and/or potentially cure patients would seem justified.

Although rare isolated perineal and small anastomotic recurrences are considered resectable, most recurrences have grown beyond this limited extent at

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the time of diagnosis. In such cases of more extensive tumor growth, if surgery is to be undertaken, more radical procedures may be required, particularly when invasion of adjacent pelvic organs, such as the uterus, vagina, bladder, or ureter, or adjacent structures, such as the sacrum, is present.[12] Previous studies suggest that results from such radical surgeries can be optimized by applying multimodality approaches including external beam radiotherapy (EBRT), sensitizing chemotherapy, surgery, and intraoperative radiation therapy.[13–20] Although overall favorable results for locally advanced and recurrence rectal cancer treated at Mayo with multimodality therapy have been reported,[18, 21–23] the following study provides a specific appraisal of results from *en bloc* sacral resection.

MATERIALS AND METHODS

From July 1990 to August 1994, 58 patients of one surgeon (HN), with locally advanced or recurrent rectal or anal cancer, underwent surgery with planned intraoperative electron irradiation (IOERT). Sixteen of these patients, underwent sacral resection as part of their procedure, and this group of 16 patients constitutes the study population. Charts were reviewed for operative and postoperative details. Patient or family contact by questionnaire provided current information on health status, including quality of life. Follow-up was available on all 16 patients. Postoperative complications were classified as mild, requiring no significant intervention; moderate, requiring medical but not surgical intervention or hospitalization; or severe, necessitating surgery, rehospitalization, or prolongation of initial hospital stay.

Eleven patients were men and five were women. Median age was 60 (range, 44–76) years. Primary tumors included 14 patients with adenocarcinomas of the rectum and 2 patients with primary cancers of the anus, including one squamous-cell and one cloacogenic carcinoma (Table 1). All 14 patients with rectal cancer had previously undergone potentially curative resection of the primary tumor, including seven low anterior resections and seven abdominoperineal resections (APR). Four of these patients subsequently developed a first local recurrence and again underwent surgery: three with previous low anterior resections underwent salvage APR and one with previous APR underwent an explorative laparotomy and was declared "unresectable." The two patients with anal cancer had not been treated surgically before sacral resection.

Table 1.
Details Regarding Primary Tumors and Previous Treatments

	No. of Patients
Primary tumors	
Rectal adenocarcinoma	14
Initial stage*	
A	2
B_1	3
B_2	6
C_2	3
Anal	
Squamous-cell carcinoma	1
Cloacogenic carcinoma	1
Previous treatments	
Surgical procedures	
Low anterior resection	7
Abdominoperineal resection	7
Reresection abdominoperineal resection	3
External beam radiation therapy	
Primary therapy component (45–60 Gy)	6
At first recurrence (54–70 Gy)	6
Presacral resection	
No prior RT (45–50 Gy)	4
Prior RT (5–45 Gy)	9
Chemotherapy	
Primary or adjuvant	6
Presacral resection	9

RT = radiation therapy.
* Astler-Coller stage[33] at time of first surgery.

All patients had received previous EBRT, 6 as a component of primary therapy (range, 45–60 Gy), 6 after the detection of the first local recurrence (range, 54–70 Gy), and 13 before sacral resection. Of the latter patients, four who had not been previously irradiated received a full course of EBRT (range, 45–50 Gy), and 9 who had previously been irradiated received an additional 5 to 45 Gy. Six patients received 5-fluorouracil-based chemotherapy as primary or adjuvant therapy, and nine received chemotherapy before sacrectomy.

For ten patients, the median recurrence interval between the time of primary surgery for rectal cancer and time of the sacral procedure was 32.5 (range, 13–51) months. For four patients, the median interval from first surgery to first recurrence was 23.5 (range, 11–37) months. The two patients with anal cancer underwent sacral resection 5 and 22 months following primary treatment with radiation and chemotherapy. Local recurrence appeared within two and three years from the primary treatment in 37.5 (6/16) and 56 percent (9/16) of patients, respectively.

Recurrences were detected by clinical evaluation of symptom presentation in 13 (81 percent) patients. Predominant presenting symptoms included pelvic pain in 12 patients and rectal bleeding in 1. Two patients had recurrent disease detected by rising carcinoembryonic antigen levels, which led to computed tomography (CT) scan, and one was detected by surveillance CT scan. Before sacral resection, all patients underwent extensive preoperative evaluation. No patient was found to have distant metastasis by physical examination, liver function studies, chest radiography, and CT scan of the abdomen and pelvis. Additional studies, including CT scans of the chest and magnetic resonance imaging of the abdomen and pelvis, were performed as clinically indicated. Large bowel studies included colonoscopy or proctosigmoidoscopy plus barium enema.

SURGICAL TECHNIQUES

Sacral resections, performed under general anesthesia, typically involved four consecutive stages, including an anterior approach, posterior approach, IOERT, and pelvic reconstruction. The anterior approach (Fig. 1) was performed with the patient in a legs up position. Cystoscopy, ureteral stent, and bladder catheter placement were performed by a urologist at the beginning of the case. Exploratory celiotomy and exposure of the pelvis were next performed to confirm the absence of extrapelvic disease and determine resectability. In reoperative cases, iliac vessels and ureters were often anatomically displaced, and pelvic fibrosis was present; therefore, the pelvic dissection was started along the distal aorta, and the vessels and ureters were dissected deep into the pelvis. Next, the anterior and lateral lines of resection were delineated, and adherent structures or organs were dissected such that they were removed *en bloc* with the posterior sacral tumor. At this juncture, multiple frozen section biopsies established the proximal sacral margin; this maneuver greatly facilitated the posterior sacral transsection.

Once the sacral lesion was determined to be resectable and dissected free from noninvolved anterior and lateral tissues, the internal iliac vessels were ligated, and gastrointestinal and/or urinary stomas were fashioned, as required. Internal iliac vessel ligation, below the superior gluteal branch where feasible, was generally performed to reduce blood loss when the sacral transsection was at or proximal to S-3. Finally, before closing the abdomen, either the omen-

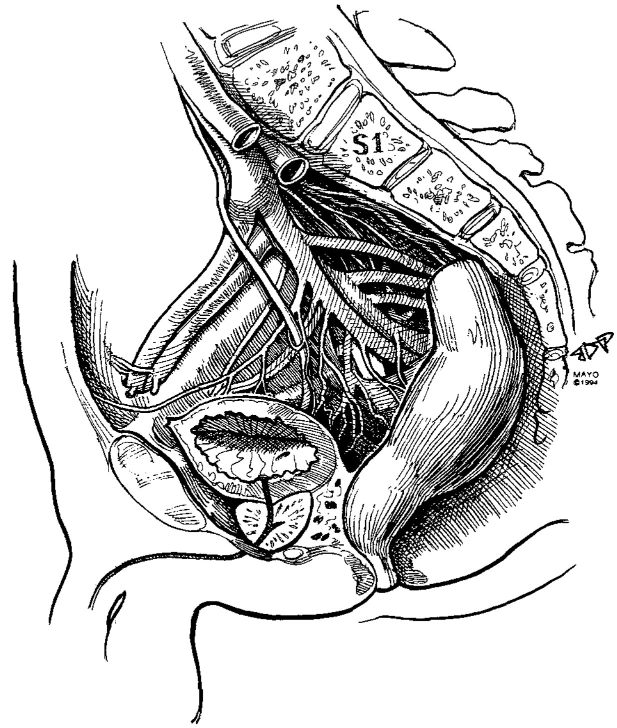

Figure 1. Operative techniques, anterior approach (operative anatomy). The anterior procedure provides assurance that no extrapelvic disease is present and provides several preparatory steps for the sacral resection, including anterior and lateral dissection, proximal sacral margin delineation, parasacral vascular ligation, gastrointestinal and/or urinary stoma formation, and omental or rectus abdominus flap creation. Reprinted with permission of the Mayo Foundation.

tum, or later in our series, the rectus abdominus flap was mobilized and placed in the pelvis for subsequent reconstructive purposes.

With the patient now repositioned, prone and flexed, a midline posterior incision was made, and the gluteus was dissected from the sacrum (Fig. 2). In rare cases, it was necessary to perform wide excision of the sacral skin and gluteus. Once the gluteus muscles were dissected for exposure, the lateral dissection was started by dividing the sacrotuberous and sacrospinous ligaments. The pyriformis muscle was divided, whereas the sciatic nerve and, if possible, the pudendal nerve were protected. Finally, the endopelvic fascia was entered, and the sacral transsection level was established. The pelvic and orthopedic surgeons typically worked together to perform the laminectomy, dural sac ligation, boney transsection, and to free the pelvic sidewalls, with cautious attention to the location of ureters, bladder, urethra, and sciatic nerves. When the tumor extended laterally, close to the pelvic sidewall, the ligaments were taken at their

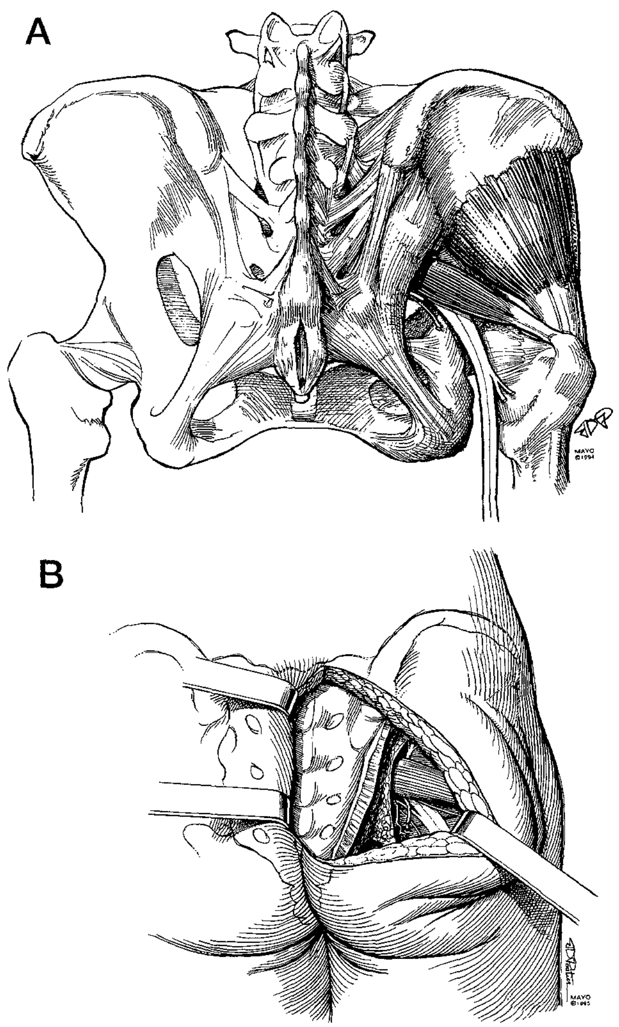

Figure 2. Operative techniques, posterior approach (A: anatomic relationships; B: operative anatomy). To remove the sacral tumor posteriorly, the gluteus must be dissected from the sacrum, and the sciatic nerve identified. The sacrotuberous and sacrospinous ligaments, pyriformis muscle, and endopelvic fascia are divided, and then the dural sac is ligated and sacrum transsected. Reprinted with permission of the Mayo Foundation.

lateral attachment to the pelvis. At times, the sacrospinous ligament was removed with a portion of the spine and pelvic sidewall to accomplish clear margins.

The specimen, removed *en bloc*, was reviewed with the pathologist and radiation oncologist to determine margins and the need for IOERT. Because the procedures were performed in a dedicated IOERT suite,[21] patients were readily repositioned beneath the linear accelerator for delivery of electron beam irradiation. Suitably sized lucite cylinders were positioned to encompass the margin of concern, and doses of between 0 and 20 Gy were delivered, depending on the extent of margin involvement. To conclude the procedure, pelvic drains were placed, and the dead space was closed with either omentum followed by gluteus and skin reapproximation or, alternatively, using a rectus abdominus flap with a skin paddle (Fig. 3).

RESULTS

In four patients sacral tumor resection alone was sufficient. In the remaining 12 patients, additional procedures were indicated for complete tumor extirpation (Table 2). Completion proctectomy was performed in all six patients who had not previously undergone abdominoperineal resection. Adherent structures and organs, most typically gynecologic or urologic, were resected as required for tumor adherence. Sacrectomy was performed through a combined anterior and posterior approach in 12 patients. In the remaining four patients, the posterior approach was not required. Two of the four patients who underwent anterior approach alone had unilateral sacral tumors with a proximal extension, requiring removal of just the anterior sacral table. The proximal level of complete sacral resection involved S2–3 in four patients, S3–4 in five patients, and S4–5 in five patients (Table 2).

When specimens were examined microscopically, surgical margins appeared clear in 11, close (2 mm) in 3, and microscopically involved in 2 patients (Table 3). Intraoperative radiation therapy was delivered to one or more fields in 14 patients with doses ranging from 10 to 20 Gy per field (Table 3). The majority of patients received a single IOERT field and a dose of at least 15 Gy. One patient with a close margin and 2 patients with clear margins required two IOERT fields to cover all sites considered at risk. Two patients had no surgical sites considered at risk and, therefore, received no IOERT.

Combined operative plus IOERT times ranged from 6 to 17 (median, 12.5) hours, and blood loss ranged from 300 to 12,600 (median, 3,350) ml (Table 4). All patients were kept one night in the intensive care unit. Length of hospital stay ranged from 11 to 30 (median, 16.5) days.

No operative deaths resulted. Eight patients (50 percent) suffered severe postoperative complications, including pelvic wound infection or dehiscence, ileal perforation, sepsis, urinary leak, and pelvic abscess. The most common severe complication involved the posterior pelvic wound. Four patients required reoperation for placement of a myocutaneous flap. Reop-

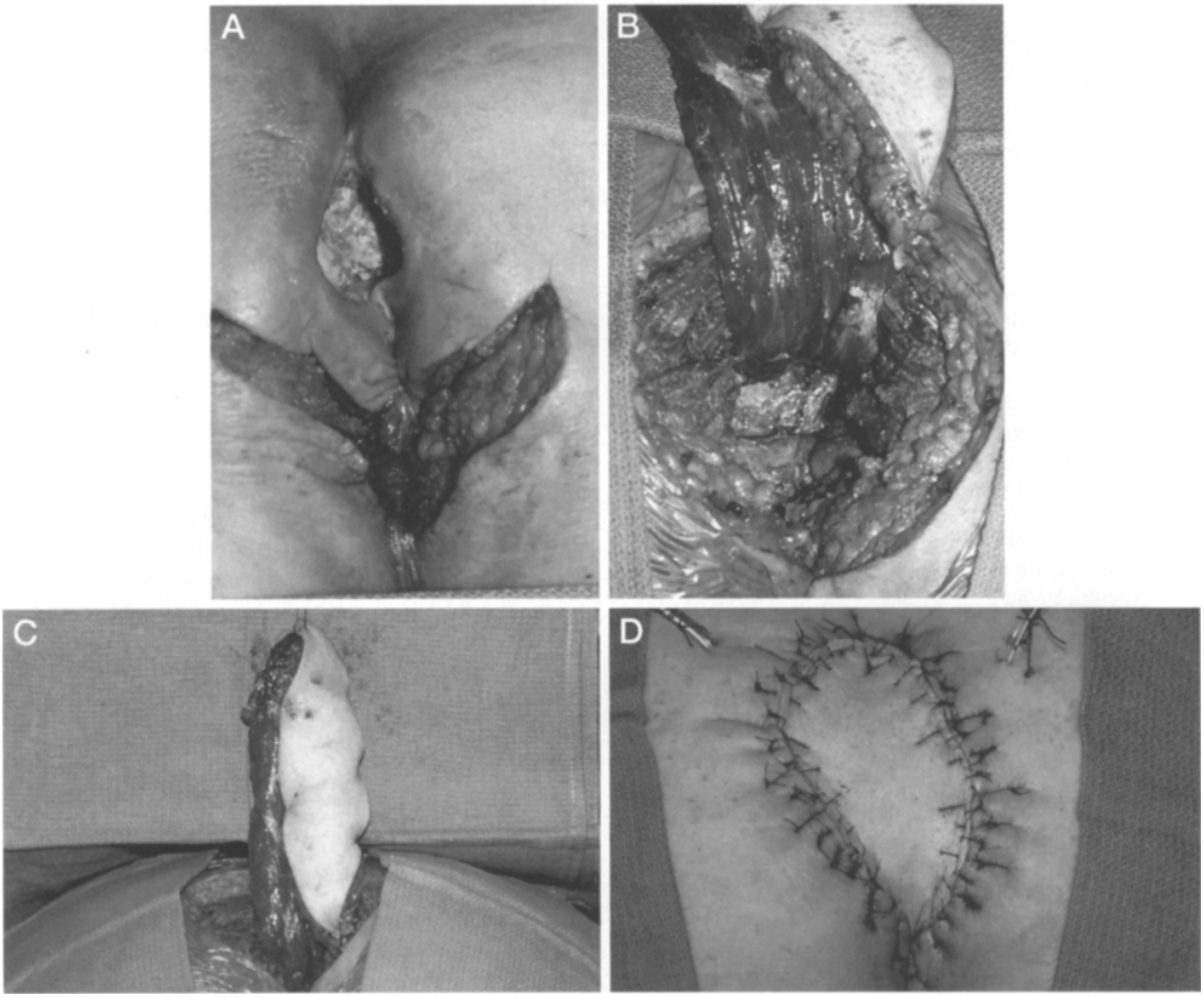

Figure 3. Operative techniques, reconstruction. Large pelvic and perineal defects from wide excisions (A) can be closed with a rectus abdominus myocutaneous flap. This recreates an abdominal-pelvic partition (B) and provides healthy, vascularized, nonradiated skin (C, D) to facilitate healing.

erative surgery was also required for an ileal perforation and pelvic abscess. Five patients (31 percent) experienced no postoperative complications, and the remaining three (19 percent) patients experienced mild to moderate complications. In 11 patients treated with single field IOERT, the complication rate was 36 percent (4/11), whereas all 3 patients (100 percent) treated with multiple field IOERT developed complications.

With a follow-up time from 2 to 37 (median, 18) months, 9 of 16 patients were alive at the time of analysis. Seven were living with no evidence of disease at 2 to 37 (2, 4, 5, 13, 15, 20, and 37) months, and one each was alive with local failure at 21 months and with distant metastasis at 9 months. Seven patients died between 5 and 33 (5, 6, 10, 11, 13, 20, and 33) months after surgery. Five died with disseminated disease, one with pulmonary metastases plus local failure, and one with local failure alone. Kaplan-Meier survival was 68 percent at one year and 48 percent at two years.

The relationship between margins and outcome was examined. Of the two patients with microscopic residual disease on surgical margins, one was alive at 13 months and one died at 33 months. Among the patients with uninvolved surgical margins, three with microscopically close margins died at 11, 13, and 20 months, three with clear margins died at 5, 6, and 10 months, and eight with clear margins were alive at 2, 4, 5, 9, 15, 20, 21, and 37 months.

Questionnaires were mailed to nine living patients. Eight (90 percent) of nine respondents indicated that

Table 2.
Sacral Resection, Operative Details

	Number of Patients
Level of sacral resection	
S2–3	4
S3–4	5
S4–5	5
Anterior table	2
Associated procedures	
Abdominoperineal resection	6
Uterus/vagina/ovaries/tubes resection	3
Cystectomy (partial or complete)	2
Ureter/seminal vesicle/prostate resection	2
Small bowel resection	2
Common iliac artery resection/graft	1
Posterior wound closure	
Primary closure	5
Omental pedicle	9
Myocutaneous flap	2

Table 3.
Sacral Resection, Oncologic Details; Pathologic Margins, Intraoperative Radiation Therapy Doses, and Fields

	Number of Patients
Pathologic margins	
Clear	11
Close	3
Positive (microscopic)	2
Intraoperative radiation therapy	
Total dose per field (Gy)	
None	2
10–12.5	4
15	6
20	7
Number of fields (17 fields per 14 patients)	
1	11
2	3

their quality of life was improved, and their cancer pain was reduced after the procedure. Six of these patients returned to their original occupation.

DISCUSSION

Although sacropelvic resection for primary chordomas is an established therapy,[24, 25] the application of this surgical approach for locally advanced and recurrent anorectal cancers is not widely practiced. The greatest proponent of sacropelvic resection for the indication of recurrent rectal cancer has been Wanebo

Table 4.
Sacral Resection, Perioperative Details

	Number of Patients
Intraoperative complications	
Urethral damage	1
Internal iliac vein laceration	1
Deaths within 30 days	0
Postoperative complications	8
Operative blood loss (median): estimated, 3,350 (range, 300–12,600) ml; replaced, 7 units.	
Operative time (median) 12.5 (range, 6–17) hours.	

et al.,[26] whose series of 53 patients is the largest to date. Remarkably, they achieved four-year cure rates of up to 33 percent when abdominal sacral resection was performed for recurrent rectal cancer with curative intent. At our institution, sacropelvic resection was performed in a manner similar to that described by Wanebo and colleagues; however, the strategies for combined modality treatments differed, principally by the use of IOERT. Before performing sacral resection, patients received either primary EBRT plus 5-fluorouracil-based chemotherapy or, if previously irradiated, they received additional radiation plus 5-fluorouracil-based chemotherapy. Immediately following sacral resection, based on margins at risk, patients received electron beam IOERT. Early results from multimodality therapy, including sacral resection and IOERT for locally advanced and recurrent anorectal cancer involving the sacrum, were reviewed.

Overall, sacropelvic resections were well tolerated. There were no postoperative deaths. The absence of mortality in this series compares favorably with previously reported mortality rates of between 0 and 9 percent.[26–29] Our favorable mortality figure may reflect a selection bias because it is our belief that the magnitude of the procedure dictates that patients should be in good physical condition. The presence of significant comorbid conditions contraindicates the procedure. Although there were no deaths in this series, one-half of the patients experienced significant postoperative morbidities. These results are in keeping with previously published morbidity rates of between 25 and 60 percent.[27, 29] Although the relative contribution of preoperative external beam and intraoperative electron beam radiation therapy to the risk of complications cannot be determined, it was observed that patients in our series treated with multiple IOERT fields were at greater risk for complications.

The higher rate of complications in patients treated with multiple IOERT fields may reflect multiple factors, including more extensive tumor spread and more aggressive surgery, rather than adverse effects from IOERT alone, as suggested by other reports.[16]

Most of the severe complications in this and other reported series[28–30] have involved posterior sacral wounds. No universally accepted closure technique guarantees success because wound problems have been noted following primary closure, advancement flaps,[29] and rotational flaps.[30] Early in our series, posterior wounds were approximated primarily, with omentum, when available, used to close pelvic defects. Following the presentation of delayed wound separations requiring reconstructive surgery, the possibility of immediate myocutaneous reconstruction with the rectus abdominus was considered. It is now current practice to perform primary reconstruction when the omentum is inadequate and a sizable pelvic defect has been created. Harvesting the rectus abdominus myocutaneous flap adds little to the overall operating time; although flap closure prolongs the length of primary hospital stay, secondary hospitalizations have been avoided. Closure techniques other than the rectus abdominus are required when simultaneous urinary and gastrointestinal stomas are surgically indicated.

Just as proper patient selection may favorably influence morbidity and mortality outcomes, it is equally important for insuring favorable cancer outcomes. Sacropelvic resection is contraindicated when complete resection is not considered possible based on preoperative studies. In general, demonstration of pelvic sidewall involvement, growth into the sciatic notch, S1/S2 involvement, and/or encasement of the bladder or iliac vessels contraindicates surgery. Furthermore, the presence of extrapelvic disease, including peritoneal or liver nodules as determined at surgery, precludes complete resection.[31, 32] Based on the presented series of 16 patients with only two cases of positive margins, it seems that local tumor extent can be accurately assessed in most cases.

Because it has previously been reported that the extent of surgical resection, complete *vs.* partial, dramatically affects local control and survival,[20] this series of patients, the majority with negative margins, would be expected to do well. At this early appraisal, the data are not sufficiently mature to examine long-term outcomes. Based on other studies, it would be anticipated that five-year cure rates would approach 18 to 33 percent.[26, 28] It would further be expected that these survival figures would exceed those reported for nonsurgical historical control populations, as demonstrated by Wanebo *et al.*[26] Although it is premature to judge survival outcomes from this combined modality approach, it would seem from the early results that good local control and palliation were accomplished.

The fact that local failure was uncommon in this series is reassuring because the rationale for adding the IOERT component of treatment was to improve local control. In the initial Mayo intraoperative radiation therapy analysis by Gunderson and colleagues,[18] which included 36 patients with locally recurrent colorectal cancer treated with EBRT, surgery, and IOERT, local failure was uncommon in the EBRT field, an absolute rate of 17 percent in the 30 patients at risk $\geq$1 year, and extremely rare in the IOERT field, 2 percent. In the more recent Mayo analysis by Suzuki *et al.*,[23] of 106 patients with palliative resection (positive margins) of locally recurrent rectal cancer, 42 received IOERT as a component of treatment. Actuarial local relapse in IOERT *vs.* non-IOERT patients was 29 *vs.* 88 percent at two years and 40 *vs.* 93 percent at three years.

In prior Mayo analyses and as well in this series, distant sites of tumor progression were the most frequent sites of recurrence.[18] It is important to recognize the benefits of local control and merits of palliation in these most difficult cancer cases. However, it is equally clear that better control of the systemic component of disease is essential if significant progress is to be made in these patients. Progress in the field of imaging and early detection of systemic disease would improve the selection process. Alternatively, advancements in the field of secondary adjuvants might slow or curtail the development of systemic disease. Secondary adjuvant therapies, such as immune therapies that have mechanisms of action differing from those of established primary adjuvant therapies, would likely be most successful. Such therapies would provide new hope for patients with recurrent colorectal cancer who have resectable locally recurrent or focal metastatic disease.

CONCLUSION

Combined modality treatment, including EBRT, chemotherapy, sacral resection, and IOERT, for locally advanced or recurrent anorectal cancers involving the sacrum is well tolerated. With acceptable morbidity and mortality, complete surgical resection can most often be achieved. The most common complication, that of posterior sacral wound infection and dehiscence, may best be managed by prevention with immediate pelvic reconstruction using the rectus abdominus myocutaneous flap. Although early results suggest that surgical resection and IOERT provide good local control and palliation, long-term results are not available. The frequent occurrence of systemic failure indicates that secondary surgical adjuvants for reresective surgery should be sought.

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