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Conservative Surgery for Low Rectal Carcinoma After High-Dose Radiation

Functional and Oncologic Results

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Objective
Using a prospective, nonrandomized study, the authors evaluated the morbidity and functional and oncologic results of conservative surgery for cancer of the lower third of the rectum after high-dose radiation.

Summary Background Data
Colo-anal anastomosis has made sphincter conservation for low rectal carcinoma technically feasible. The limits to conservative surgery currently are oncologic rather than technical. Adjuvant radiotherapy has proven its benefit in terms of regional control, with a dose relationship.

Methods
Since June 1990, 27 patients with distal rectal adenocarcinoma were treated by preoperative radiotherapy (40 + 20 Gy delivered with three fields) and curative surgery. The mean distance from the anal verge was 47 mm (27–57 mm), and none of the tumors were fixed (15 T2, 12 T3).

Results
Mortality and morbidity were not increased by high-dose preoperative radiation. Twenty-one patients underwent conservative surgery (78%—17 total proctectomies and colo-anal anastomoses, 4 trans-anal resections). After colo-anal anastomosis, all patients with colonic pouch had good results; two patients had moderate results and one patient had poor results after straight colo-anal anastomosis. With a mean follow-up of 24 months, the authors noted 1 postoperative death, 2 disease-linked deaths, 1 controlled regional recurrence, 2 evolutive patients with pulmonary metastases, and 21 disease-free patients.

Conclusions
These first results confirm the possibility of conservative surgery for low rectal carcinoma after high-dose radiation. A prospective, randomized trial could be induced to determine the real role of the 20 Gy boost on the sphincter-saving decision.

Currently, abdominoperineal resection (APR) represents the standard surgical treatment of lower-third rectal carcinoma.[1,2] The justification for this lies in the natural history of these tumors—the high risk of local recurrence,[3] the need for a 2-cm distal margin,[4,5] and the desirability of complete removal of the perirectal fat.[6,7] In recent years, improvements in surgical technique have made sphincter conservation for low rectal carci-

Table 1. PATIENT CHARACTERISTICS

No. of patients	27
Female	12
Male	15
Age	Range 29–78 yr; median 65 yr
Astler Coller's classification	
T-	4
A	0
B1	15
B2	2
C2	5
D	1
Clinical distance of lower tumor margin from anal verge	
<2.9 cm	5
3–4.9 cm	18
5–6 cm	4
High-dose preoperative radiation (60 Gy)	27
Surgery	
Straight colo-anal anastomosis	3
Colo-anal anastomosis with J pouch	14
Abdominoperineal resection	6
Transanal resection	4
Postoperative chemotherapy	6
Follow-up period	Range 6–42 mo; median 24 mo

noma technically feasible. Colo-anal anastomosis (CAA) was first described by Sir Alan Parks[8] more than 20 years ago. The limits to conservative surgery[1] currently are oncologic rather than technical, with concerns about the risk of local recurrence and possible reduced survival.

For more than 20 years, we have used preoperative adjuvant radiation for invasive rectal cancer, using a dose of 40 Gy.[9] The benefit of this additional treatment in terms of improving locoregional (LR) control currently is being demonstrated.[10–13] Evidence for a dose relationship[14] on LR control led us further to propose a 20-Gy boost to patients with lower-third rectal tumors. This high-dose preoperative radiotherapy has allowed sphincter preservation in good responders. This article analyzes the functional and oncologic results of this treatment. The data will be compared with those in the literature.

METHODS

Clinical Material (Table 1)

Since 1990, we have routinely offered high-dose preoperative radiation to patients with distal rectal adenocarcinoma, within 6 cm of the anal edge. These were patients who would otherwise have been treated primarily with APR, and all of them accepted preoperative radiation. At the Montpellier Cancer Institute from June 1990 to June 1993, we studied 15 men and 12 women with low rectal cancer, with a mean age of 65 years.

Pretreatment investigations included clinical examination, endorectal ultrasonography, tomodensitometry and magnetic resonance imaging, chest radiography, liver ultrasonography, and tumors markers. Cystoscopy was performed on patients with anterior tumors. On histologic examination, we found 26 adenocarcinomas (16 were well differentiated, 8 were moderately well differentiated, and 2 were undifferentiated) and 1 colloid carcinoma. Ninety percent of the tumors involved less than the half of the lumen, and none were fixed.

Before radiotherapy, we estimated tumor rectal wall invasion according to the TNM system of the Union Internationale Contre le Cancer; no patient had a T1 tumor, 15 had T2 tumors, and 12 had T3 tumors. Five patients had clinical suspicion of lymph node involvement, one patient had a solitary liver metastasis. The length between the tumor inferior pole and the levator ani was assessed by rectal examination during voluntary contraction, by endorectal ultrasonography, and by frontal section of magnetic resonance imaging. The average distance was 17 mm (range = 0–27 mm). The mean distance from the anal verge was 47 mm (range = 27–57 mm). In four patients, the inferior pole was located at the superior end of the sphincter ring.

Therapeutic Methods

Preoperative radiotherapy was performed with a linear accelerator (25 MEV). The target cells were the tumor, the perirectal fat, and the regional nodal chains. The center of this target was assessed after comparing the results of rectal examination, barium opacification, and pelvis scanning. Radiation was delivered with three fields—one posterior and two lateral. First, a classical 40-Gy radiation was given (18 × 2.1 Gy, i.e., 37.8 Gy over 3 weeks). After a 3-week break, radiosensitivity was evaluated by repeating the pretreatment investigations. Patients with tumor reduction of at least 30% had a tumor boost to reach a biologic dose of 60 Gy. Patients with unchanged tumor underwent APR.

Surgery was performed 2 to 4 weeks after completion of the tumor boost. For tumors located above the anal sphincter, surgical resection was performed classically by an abdominal approach. Regional lymph nodes along the inferior mesenteric vessels and front the aorta were examined intraoperatively. The splenic flexure was mobilized completely in all cases. The entire rectum was dissected to the levator floor, exposing the levator muscles.

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The inferior rectal section was done under traction close to the levator ani. The specimen was open immediately to determine both macroscopic and microscopic resection margins. Sphincter integrity always was checked. Abdominoperineal resection was performed on one occasion because of injury to the anal sphincter. Perineal time removed the anal mucosa until the pectinate line and the internal sphincter. Bowel function was restored by CAA,[8] most often with a J colonic pouch.[7,15,16] Defunctioning colostomy was performed routinely.

Transanal resection (TAR) also was performed for radiosensitive tumors initially located through the sphincter,[2] and APR was performed where resection margins were positive.

Chemotherapy (consisting of 5 FU and folinic acid) was given for tumors with nodal metastasis (Dukes' C).

Assessment of Functional Results

This assessment included clinical and manometric criteria. Clinical criteria were daily stool frequency, urgency, discrimination between flatus, liquid and solid stools, type of continence (normal, minor, and major leak). All these data were combined to produce a comprehensive functional assessment.[17]

Outcomes were as follows: a good outcome—no urgency and no incontinence, 1 to 2 daily stools, or constipation; a moderate outcome—no liquid or solid incontinence, but possible urgency or 3 or 4 daily stools; a poor outcome—combined urgency and incontinence or more than 5 daily stools. Manometric examination, using Arhan's catheter, was performed systematically before closure of the defunctioning colostomy. Sphincter assessment included resting anal pressure, voluntary contraction, and functional length. Neurosensory function was assessed by demonstration of the recto-anal inhibitory reflex and measurement of the distension threshold. Neorectal compliance was evaluated by balloon insufflation, with measurement of maximum tolerable volume and rectal sensitivity threshold volume.

Patient Follow-Up

All the patients included in this protocol had quarterly visits during the first 3 years after treatment, then 6 monthly visits until the fifth year, then yearly visits. Clinical examination, tumor marker assays, liver ultrasonography, and chest x-rays were performed routinely. Six-monthly endorectal ultrasonography, alternating with abdominopelvic computed tomography scan and yearly coloscopy also were performed. The follow-up period ranged from 6 to 42 months (median = 24 months); all patients were able to be observed for follow-up.

RESULTS

Mortality

No patient died during radiotherapy. One patient died the day after APR from acute myocardial infarction.

Morbidity

Five patients (18%) received treatment for gastrointestinal or genito-urinary symptoms (diarrhea, rectitis, cystitis) during radiotherapy. Postoperative complications included temporary dysuria and vesical denervation, occurring mostly in men. All patients recovered normal urinary function by the time of their first follow-up visit, 3 months after initial surgery. One patient was treated for pulmonary embolism. After APR, one patient had a breakdown of the perineal wound. Median hospitalization was 21 days—23 days after CAA, 20 days after APR, and 17 days after TAR. One patient developed a symptomatic anastomotic stricture, requiring dilatation under neuroleptanalgesia. Asymptomatic anastomotic strictures were dilated during surveillance rectal examination in several cases. Seventy-five percent of men had sexual troubles, including erection dysfunction (30%) and retrograde ejaculation (100%).

Radiosensitivity

Assessment of tumor response to high-dose radiation was done just before operation. Two patients had no residual tumors, and lesion size was reduced by more than 80% in 9 patients and by more than 50% in 14 patients. The potential for sphincter preservation was evaluated at each stage of treatment. Conservative treatment was possible 3 weeks after completion of the first course (40 Gy) in 3 cases, 2 weeks after 20-Gy boost in 15 cases, and preoperatively in 3 cases. According to Astler-Coller staging, at the time of surgical removal, 4 tumors had been sterilized completely, 15 were B1 lesions, 2 were B2 lesions, and 6 were C2 lesions. One patient had a left lobectomy for a solitary liver metastasis.

Sphincter Conservation

Preoperative staging indicated that conservative surgery was possible in 25 cases; however, it was done in only 21 patients (78%). Six APRs were performed; three times, the levator ani was macroscopically found to be involved, in one patient a positive resection margin was found, in one patient, tumor excision necessitated removal of part of the levator ani, and in the last patient, APR was required for bleeding associated with anticoagulation. Conservative surgery consisted of total proctectomies and CAA for 17 patients (3 straight CAA and 14

Table 2. FUNCTIONAL RESULTS AFTER COLO-ANAL ANASTOMOSIS

Kirwan's continence classification[14]	
1) Perfect	10
2) Incontinent to gas	2
3) Occasional minor leak	2
4) Frequent major soiling	0
5) Colostomy	0
Bowel movements	
Constipation	3
1 or 2 per day	9
3 to 5 per day	1
>5 per day	1
Urgency	2
Urinary dysfunction	
Postoperative	12
After 1 month	2
After 3 months	0
Sexual dysfunction (13 men evaluated)	
Anerection	4 (30%)
Sexual weakness	3 (23%)
Retrograde ejaculation	13 (100%)

14 patients studied with a mean follow-up of 14 months; 3–28 mo.

colonic pouch). In 4 patients, TAR was performed; 2 of these patients were elderly (77 and 78 years old), and 2 had very low tumors, a complete response, and refused permanent colostomies. In all, these patients histologic margins were clear. Mean safety margin after CAA was 16.8 mm (range = 12–21 mm).

Functional Results After CAA (Table 2)

All patients were continent preoperatively, with a median stool frequency of 1.2. Median functional follow-up is 14 months after closure of the defunctioning colostomy (performed on average 68 days after CAA); 14 patients were evaluated. Stool frequency ranges from 1 every 2 days to 6 daily, with a mean stool frequency of 1.6. Stool frequency appears to depend on the type of surgery used—i.e., one daily stool or constipation after colonic pouch and two to four daily stools after straight CAA. These data change very little with increasing follow-up. All CAA and TAR patients are continent for solid stool, whereas two patients report incontinence for gas or liquid stool. Two patients after straight CAA have stool urgency not helped by conventional medication. All patients who had CAA with colonic pouch had good results, whereas two had moderate results and one had poor results after straight CAA.

Manometric assessment was performed routinely before restoration of digestive function, usually on the 14th week after CAA. Sphincter function was good with a mean resting anal pressure of 23 cm (normal: 25 cm) and a functional length of 2 cm (normal: 2 cm). The recto-anal inhibitory reflex was not seen because of routine dissection of the internal sphincter. The recto-anal excitatory reflex and distension thresholds were within the normal range. Neorectal compliance depended on surgical technique: rectal sensitivity threshold volume ranged from 48 mL for straight CAA to 70 mL for CAA with colonic pouch (normal: 60–120 mL), and the maximum tolerable volume ranged from 80 mL to 150 mL (normal: 150–300 mL).

Oncologic Results (Table 3)

Mean follow-up from beginning of radiation therapy is 24 months (range 6 to 42 months).

One patient developed an obstructive local recurrence 10 months after CAA and J pouch. This was for a non-fixed stage C2 colloid cancer. Tumor response to radiotherapy had been 50% reduction, and the safety margin was 15 mm. Recurrence was high and posterior, at the level of the sacral promontory, not involving the anastomosis and without distant metastases. Combined treatment included posterior pelvectomy with a 30-Gy radiation boost to the sacral area and chemotherapy (5 FU and folinic acid). The patient died from regional evolution 4 months later. One patient had a regional recurrence 11 months after TAR procedure for an initially T3 tumor, and sterilized after 60 Gy. A curative APR was performed. Three patients had pulmonary metastases—one during chemotherapy for a stage C2 carcinoma (CAA), two 11 and 26 months after surgery (1 CAA and 1 APR done for wounded sphincters).

The survival curve was calculated by the Kaplan-Meier method. It was 83% at 2 years. In 27 patients, after 24 months mean follow-up, we noted 1 postoperative death, 2 disease-linked deaths, 1 controlled regional recurrence, 2 evolutive patients (pulmonary metastases), and 21 disease-free patients.

Table 3. CLINICAL RESULTS

Distance of the lower tumor edge from margin of resection (range 12–21 mm; median 16.8 mm)		
Postoperative mortality	1	
Postoperative morbidity	2	
Hospitalization (range 12–53 days, median 21 days)		
Colostomy closure after CAA	14/17	
Present status		
No evidence of disease	21	80.7%
Regional recurrence	2	7.6%
Distant metastasis	3	11.5%

DISCUSSION

Data reported in literature compare local control and survival after APR and sphincter-saving procedure of upper and mid-rectal cancer only. The possibility of extending restorative techniques to tumors of the lower third of the rectum have been considered only more recently in a limited number of studies.[6,7,18–23]

Adjuvant radiotherapy has become standard practice in the treatment of high-risk rectal carcinoma, particularly for low tumors beyond stage B1.[13] Preoperative radiation results in less morbidity and better local control than postoperative radiation.[11,24] Experiments have shown a relationship between radiation dose and tumor response.[14,23,25] Clinical series confirm poor results for preoperative radiation of less than 20 Gy,[10,25] but improved local control using doses of 40 Gy or higher.[9,12,26–29] Published data on high-dose radiation and sphincter conservation for initially low but resectable rectal carcinoma are rare. Papillon[30,31] demonstrated the benefit of intracavitary radiation for early grade lower rectal carcinoma (A, B1) and of high-dose preoperative radiation with conservative surgery for more advanced lesions. Marks,[19–21] Mohuiddin,[22,23] and Cohen[18] reported the possible use of high-dose radiation for middle- and lower-third rectal carcinoma. Our results were compared with those in the literature.

Morbidity

Preoperative radiation of lower-third rectal carcinoma does not result in significant morbidity. Except for Stevens' experiment,[32] our results agree with those of the large series in the literature.[11,12,33] Tumor boost does not increase the incidence of preoperative gastrointestinal symptoms or lead to increased postoperative sequelae. No patient was forced to stop the irradiation because of gastrointestinal or urinary symptoms. Operative difficulty did not increase with high-dose radiation, and anastomotic safety appeared to depend on colonic vascularization rather than radiation sequelae.[34]

Sphincter Preservation

Sphincters were preserved in 78% (21/27) of patients after high-dose radiation. All of these tumors would have required APR if they had been resected immediately. Only 3 tumors would have allowed sphincter preservation 3 weeks after the conventional 40-Gy radiation. Amenability to conservative surgery depends on a longer interval between radiotherapy and surgery and, above all, an increased tumor response linked directly to higher radiation doses.

Gathered information from rectal examination, endorectal ultrasonography, pelvic tomodensitometry, and magnetic resonance allow an assessment of the response to radiation therapy and the potential for sphincter preservation. Dynamic rectal examination during voluntary sphincter contraction helps to determine the relationship between the inferior level of the tumor and the levator ani. The frontal views of the magnetic resonance imaging also are useful. Evidence of tumor radiosensitivity was seen in all 21 patients, ranging from 50% to 100%.

Sphincter preservation after high-dose radiotherapy brings into question many of the assumptions used to justify the use of APR in the treatment of low rectal carcinoma.

Tumor radiosensitivity is an important prognostic factor that cannot be determined where postoperative irradiation is used. This has been proven for classical 40-Gy preoperative radiation.[3] Tumor radioresistance is of more prognostic significance after high-dose radiation.[22,23]

The accepted safety margin for inferior rectal section should be re-addressed. The standard 2-cm margin is based on anatomicopathologic studies that always have been done for primarily operated tumors.[4,5] In our study, the mean safety margin was smaller than to 2 cm (mean 16.4 mm). Wolmark and Fischer[35] report the same survival for rectal tumors resected with distal margins of less than 2 cm compared with those greater than 3 cm, although local recurrence may be of more importance than crude survival (NSABP R01). Pollet and Nicholls[4] found the same results for survival and local recurrence comparing margins of less than 2 cm and greater than 2 cm. Mohuiddin[22] published on 26 patients having sphincter preservation for tumors less than 6 cm from the dentate line. The mean safety margin was 15 mm, resulting in an LR rate of 11% and 72% survival at 5 years.

At sphincter level, removal of perirectal tissue is less complete after conservative surgery than APR. Effective radiotherapy allows sphincter preservation by sterilization of tumor deposits in the perirectal tissue. Above the sphincter, quality of removal is the same as for APR or CAA.[7,36] A careful perirectal soft-tissue dissection appears to be the most determining factor in minimizing pelvic relapses.[6] Furthermore, free histologic margins remain very important, and a positive result on frozen section during rectal removal mandates APR.[1]

Functional Results

Functional results are not altered greatly by preoperative radiation, particularly compared with postoperative radiation.[11] Boost has little effect on function because it is delivered only to the tumor bed. Radiation-induced fibrosis reduces maximum tolerable volume and rectal

sensitivity threshold volume. Neorectal compliance is rendered normal because of creation of a colonic pouch. We believe that functional results and quality of life are linked to surgical technique rather than to boost. Coloanal anastomosis with colonic pouch gives better results with regard to stool frequency and urgency than straight anastomosis, and this does not change with extended follow-up.[15,16,37-39]

Locoregional Recurrence

Mean follow-up is only 24 months in this study, and therefore, analysis of outcome must be cautious. At the time of writing, LR rate was only 7.4%, which is the same as for a retrospective study of 111 patients treated in our institution by 40-Gy preoperative radiation and APR.[9,26] In the literature, LR rates for low rectal carcinoma treated by APR and radiation ranged from 9% to 15%.[11,12,25,35] In case of sphincter preservation, LR rates after surgery alone are very disparate, ranging from 3.5%[6] to 20.6%.[8] After high-dose radiation, these data range from 5% to 11%.[18,22,30] In our study, the 2 LR recurrences initially had high-risk parameters—one colloid carcinoma T3N+ and one adenocarcinoma T3 treated by TAR. The two recurrences were regional, once in the promontory, the second 7 cm above the first lesion, in the rectal wall without mucosa involvement. Lateral safety margins are as important as distal safety margin,[1,7] and therefore, radical proctectomy with CAA is performed most often in our institution rather than TAR. Moreover, early diagnosis of LR recurrence is easier after CAA than after APR.

Survival

Final results of the EORTC trials,[12] published in 1988, showed no statistically increased survival after preoperative radiation (59% *vs.* 69%; p: 0.08). There was a significant difference in survival, however, for patients younger than 55 years of age (80% *vs.* 48%). Many prospective randomized studies reached the same conclusions.[10,11,13]

Conversely, many retrospective studies show evidence of increased survival of preoperatively irradiated patients.[2,3,23,26-30,40] Better local control of a disease in which isolated locoregional evolution kills more than one third of patients should improve survival. Evidence from this study, that conservative surgery for low rectal tumors after high-dose radiation does not reduce survival, may be of great significance, particularly if this can be achieved with either the same local control rate or with an early diagnosis of LR recurrence. Our early results and data in the literature[7,18,21,22] are encouraging, but longer follow-up is necessary.

CONCLUSION

In 1939, Dixon[41] published the first sphincter preservation for upper rectal carcinoma. In 1984, Williams[42] confirmed the possibility of sphincter-saving resection for carcinoma of the middle third of the rectum. Ten years later, validity of this surgery is being discussed for tumors of the lower third of the rectum.[43] We can conclude on the technical feasibility of this surgery after high-dose radiation, but these first results should pass the test of time to confirm its oncologic safety. A prospective, randomized trial could be induced to determine the real role of the 20-Gy boost on the sphincter-saving decision.

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