ORIGINAL ARTICLE

Total Mesorectal Excision and Low Rectal Anastomosis for the Treatment of Rectal Cancer and Prevention of Pelvic Recurrences

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Hypothesis: Total mesorectal excision lowers the rate of pelvic recurrence and positively affects the survival after surgical treatment of rectal cancer.

Design: Case series.

Setting: Tertiary care university hospital.

Patients: Fifty-three consecutive patients were admitted with curative intent to surgery at the First Department of Surgery of the University of Rome "La Sapienza," Rome, Italy, with diagnoses of rectal carcinoma. The mean follow-up was 68.9 months; follow-up was complete for all patients who entered the trial.

Interventions: Low anterior resection and total mesorectal excision were performed in all cases, regardless of the location of the rectal cancer. A straight mechanical colorectal anastomosis was performed on a rectal stump, never exceeding 5 cm. No kind of adjuvant therapy was given. Mesorectum and open rectum were studied by serial transverse section at 5-mm intervals. A search for depth of penetration and distal intramural extension of the tumor was made. Lymph nodes were detected by clearing method, and nodal metastases (NM) and nonnodal metastases (NNM) were recorded as situated proximally, distally, or at the level of the tumor.

Results: There was no postoperative mortality. Clinical and radiologic leaks occurred in 2 and 4 patients, respectively. Mean disease-free survival was 65.9 months. Pelvic recurrence occurred in 5 patients (9%). Overall 5-year survival rate was 75%. Involvement of mesorectum by NM and NNM was detected in 27 and 24 cases, respectively. Both NM and NNM were found to be distal in 33% and 40% of cases, respectively.

Conclusions: Microscopic spread to the distal mesorectum may exceed the intramural spread of rectal cancer. Failure to perform total mesorectal excision leaves a potentially residual disease in the distal mesorectum, thus predisposing the patient to pelvic recurrence.

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PELVIC RECURRENCE following curative surgery for rectal cancer is common, ranging between 5% and 45%.[1-4] This considerable variation in different series is probably due to differing quality of surgical treatment.[3,4] It is increasingly believed that many of these local recurrences are due to incomplete excision of metastatic deposits scattered in the supporting structures around the rectum.[1,3,5,6] Most frequently, local cancer spread discontinuous with the primary rectal tumor takes place in the mesorectal lymph nodes (nodal metastases [NM]). However, nonnodal metastases (NNM), which have been described in other organs,[7] have been found within the mesorectum and outside it along lateral pelvic vessels, autonomic nerves, and the pelvic wall.[1,2,5,7-9] Our aim was to determine the incidence of NM and NNM, their relation to other clinicopathologic characteristics, and their influence on survival and recurrence rate in patients treated with curative low anterior resection (LAR).

RESULTS

CLINICAL AND PATHOLOGIC DATA

The mean distance of the tumor from the anal verge was 10.6 cm (SD, 1.7 cm). There were 13 patients with Dukes stage A disease, 24 with stage B disease, and 16 with stage C disease. The mean distance of the tumor from the surgical resection margin was 5 cm (SD, 1.6 cm). Mean operating time was 156 minutes (range, 120-230 minutes). Clinical and demographic data are summarized in **Table 1**. Involvement of the mesorectum by NM and NNM was detected, respectively, in 27 and 24 cases. The mean number of examined

PATIENTS AND METHODS

PATIENTS

A prospective study was performed from January 1990 to December 1995. Fifty-three consecutive patients who underwent curative surgery for adenocarcinoma of the rectum consented to recruitment. Distance from anal verge was measured with a rigid proctosigmoidoscope in the left-lateral Sims position.

SURGERY

Fifty-three LARs were performed regardless of the location of the tumor. In this operation, the abdomen is entered via a midline laparotomy. Sigmoid and descending colon were mobilized by incising the lateral peritoneal attachment, and the greater omentum was extensively separated from the transverse colon along the correspondent avascular plane to completely release the proximal stump for a tension-free anastomosis. The inferior mesenteric vessels were ligated at their origin, and a complete lymphadenectomy was performed along the adventitial surface of the aorta while adopting a nerve-sparing procedure. The rectum was then mobilized and the avascular presacral space developed, taking care not to enter the mesorectum, which was entirely excised en bloc. For all tumors, dissection was carried to the pelvic floor. Lateral dissection was carried out by dissecting at the sidewall of the pelvis the supporting structures around the rectum in a square fashion, again down to the pelvic floor, to achieve adequate circumferential clearance. Anteriorly, the prostata or the vagina were mobilized, thus proceeding the dissection within the endopelvic fascia. In no case did opening of the rectum occur. In all cases, an R0 resection was attempted. The length of the rectal stump was always left at less than 5 cm to be as congruous as possible with the doubtful blood flow deriving from the sole inferior mesenteric artery. Intestinal continuity was restored by means of a mechanical straight anastomosis. Filling of the presacral space and protection of the anastomosis were achieved with the preserved intact omentum, and drainage of the anastomotic site was provided in all cases. No protective stoma was ever performed or adjuvant therapy given.

PATHOLOGY

The fresh specimen was opened on the antimesenteric border or, when the lesion was anterior, lateral to the tumor. Mesorectum and the open rectum were pinned to a corkboard and fixed in 10% formaldehyde solution. Transverse sections were carried along the rectal wall and mesorectum at 5-mm intervals. All specimens were examined by the same pathologist (L.S.) and assigned a Dukes and TNM stage (American Joint Committee on Cancer *Cancer Staging Manual*). A search for depth of penetration and distal intramural extension of the tumor was made. The distal clearance margin from the lower tumor border, grading of the tumor, vascular and perivisceral infiltration, and tumoral and peritumoral lymphatic infiltration were assessed. Lymph nodes were detected by the clearing method. Presence of NM and NNM in the mesorectum was recorded as situated proximally, distally, or at the level of the tumor.

EARLY OUTCOME

Postoperative course was monitored, and minor and major complications were recorded. Particularly, temperature, air and feces passage, blood cell count, and fecal discharge from the surgical drainage were noted to detect clinical anastomotic leakage. Between the 7th and 10th postoperative days, plain and contrast radiographs were taken to assess staple-ring integrity and anastomotic leakage.

LONG-TERM OUTCOME

During follow-up, each patient was evaluated for tumor recurrence every 3 months during the first year and every 6 months thereafter. Follow-up evaluation included history, physical examination, endoscopy, blood cell count, liver function test, and serum carcinoembryonic antigen testing. Ultrasonographic abdominal scans and chest radiographs were performed yearly. Functional outcome was assessed by evaluating the frequency and characteristics of bowel movements and anal continence.

STATISTICAL ANALYSES

Data from all patients were prospectively collected in a computerized database. Statistical analyses were performed with Statistica 5 '97 (Statsoft Inc, Tulsa, Okla) performing χ^2 tests and t tests when required. A 2-tailed $P<.05$ was considered statistically significant. The product-limit method (Kaplan-Meier) was used to analyze patient survival and patterns of recurrence. Multivariate analyses performed to identify independent determinants of survival and recurrence were performed to analyze the following clinicopathologic variables: age, sex, size of tumor, pattern of tumoral growth, depth of penetration of tumor, vascular and perineural invasion, lymph node involvement, and NNM presence.

nodes per patients was 19.7 (range, 7-33; SD, 7.5) in patients with pT2 disease and 21.1 (range, 0-39; SD, 10) in patients with pT3 disease. The mean number of metastatic nodes was 3.3 (range, 0-14; SD, 4.3) in patients with pT2 disease and 7 (range, 0-27; SD, 9) in patients with pT3 disease. The contemporary presence of NM and NNM was detected in 16 patients. Isolated NM and NNM were detected in 11 patients and 8 patients, respectively. Nodal metastases were found to be cranial or at the same level of the rectal cancer in 67% and distal in 33% of cases. The site of NNM was at the level or cranial to the tumor in 60% of patients and distal in 40%.

Correlations between mesorectal deposits (NM and NNM) and other considered parameters are reported in **Table 2**.

EARLY OUTCOME

Four major and 8 minor complications were observed during the postoperative course. Staple-ring disruption was

observed in 5 cases. Clinical leakages occurred in 2 patients, and radiologic leakages were detected in 4 contrast-enema controls. The following tabulation details postoperative morbidity.

Complication	No. of Patients
Clinical leakage	2
Pneumonia	1
Cardiac arrhythmia	1
Wound infection	2
Urinary tract infection	1
Prolonged ileus	1
Radiologic leakage	4

LONG-TERM OUTCOME

During a mean follow-up of 68.9 months (range, 17-95 months; SD, 20.28 months), a mean disease-free survival of 65.9 months was observed (range, 6-95 months; SD, 24.14 months). Pelvic disease recurrence occurred in 5 patients (9%). Nine patients died due to progression of neoplastic disease. Four patients died due to unrelated causes. The overall 5-year survival rate was 75%. Stage-specific survival rates were 100% for Dukes stage A, 80% for stage B, and 61.5% for stage C. Patients had a median daily stool frequency of 4 (range, 3-7); other functional results are summarized below.

Function	No. of Patients
Hard stool consistency	37
Soft stool consistency	10
Liquid stool consistency	6
Incontinence	2
Urgency	13
Sensation of incomplete defecation	9
Impaired social life	2

Univariate analyses showed NNM, nodal stage, tumor size, and lymphatic tumoral infiltration as factors that influence local recurrence, whereas NNM, Dukes stage, local recurrence, and tumor size were factors influencing survival (**Table 3**). Multivariate analyses failed to confirm the former statistical correlation, showing NNM ($\beta = -0.7$, SE $\beta = 0.2$; $B = -0.69$, SE $B = 0.18$; $t = -3.8$; $P < .001$) and local recurrence ($\beta = -0.38$, SE $\beta = 0.13$; $B = -26.6$, SE $B = 9.14$; $t = -2.91$; $P < .006$) as factors influencing the long-term outcome.

COMMENT

Pelvic recurrence following perivisceral dissection of the rectum occurs with a worldwide incidence of at least 20%.[2,3,8,10-12] Intraoperative seeding of neoplastic cells and incomplete excision of the primary tumor and regional neoplastic deposits are currently considered as the main causes of local recurrence following curative surgery for cancer of the rectum.[5,6,13] The evidence of distal involvement of the mesorectum being more common than intramural distal spread has suggested the need for reconsideration of some technical aspects of the curative surgery of rectal cancer.[4,8,11,14] When compared with the standard perivisceral procedure, total mesorectal excision (TME) has been shown to achieve a more accurate staging and locoregional control of the neoplastic disease, lower the rate of local recurrence, and improve survival rates.[6,8,9,11,15,16] Yet TME has been called into question as an awkward and time-consuming procedure that leads to high leakage rates, the need for routine proximal diversion, and unfavorable functional results.[10,12,15-20]

However, in our experience, by using the procedures detailed by Heald et al[11] and MacFarlane et al,[6] dissection of the mesorectum has proven to be straightforward, because the mesorectum develops along a

Table 1. Clinical and Demographic Data*

Age, mean ± SD, y	65 ± 9.2
Sex	
Male	28
Female	25
TNM staging	
I	18
II	6
III	27
Dukes stage	
A	13
B	11
C	27
Tumor staging	
T0	2
T1	8
T2	24
T3	18
T4	1
Lymph node staging	
N0	26
N1	8
N2	15
N3	4
Total lymph nodes, mean ± SD	19.3 ± 8.8
Nodes positive, mean ± SD	4.0 ± 6.4
Grading	
Good	8
Fair	34
Poor	9
Mesorectal nodes positive	
Present	16
Absent	37
Neoplastic islets	
Present	20
Absent	33
Tumor diameter, mean ± SD, cm	4.4 ± 1.7
Distance of tumor from the anal verge, mean ± SD, cm	10.5 ± 1.6
Distance of tumor from the section edge, mean ± SD, cm	5.0 ± 1.6
Pattern of tumoral growth	
Infiltrating	23
Pushing	14
Mixed	14
Perineural invasion	
Present	14
Absent	37
Peritumoral lymphatic invasion	
Present	34
Absent	17
Tumoral lymphathic invasion	
Present	31
Absent	20
Vascular invasion	
Present	15
Absent	36

*All values are number of patients unless otherwise indicated.

Table 2. Correlation (*P*) Between Variables and Mesorectal Involvement

Variable	Neoplastic Islets	Nodal Metastasis
Nodal staging	<.003	<.0001
Pattern of tumoral growth	<.001	.61
Lymphatic tumoral invasion	<.03	.11
Total lymph nodes	<.008	<.0001
Lymph nodes positive	<.0002	<.00001
Distance from anal verge	<.001	<.02
Distance from section edge	<.002	<.02
Tumor stage	.19	<.0001
Tumor grade	.27	<.01
Tumor diameter	1.0	<.0002
Dukes stage	<.002	<.003

Table 3. Univariate Analyses *P*

Pathologic Features	Local Recurrence	Survival
Nodal metastases	<.02	.06
Nonnodal metastases	<.03	<.001
Distal level of mesorectal involvement	<.03	<.001
Nodal stage	<.05	.11
Pattern of tumoral growth	.14	.13
Lymphatic tumoral invasion	<.05	.08
Total lymph nodes	.07	.08
Lymph nodes positive	<.05	.06
Distance from anal verge	.21	.78
Distance from section edge	.22	.83
Tumor stage	.55	.20
Tumor grade	.25	.39
Tumor diameter	<.04	.06
Dukes stage	.33	<.001

well-defined avascular root. Pelvic bleeding and the neoplastic and septic contamination of the operative field consequent to intraoperative perforation of the rectum and breaching of the mesorectum are the main pitfalls described to occur frequently during the perivisceral procedure. Such complications, which are only rarely reported to occur during TME,[10,21,22] were never registered in our series. Moreover, by widening the pelvic space and achieving a more extensive mobilization of the rectal stump, TME greatly eases the anastomotic procedure. A routine defunctioning stoma has been recommended because this decreases the leakage rate of colorectal anastomosis. Although no intestinal diversion was ever provided in our series, a low rate of leakage was observed. The complete mobilization of the transverse colon and consequent releasing of the proximal anastomotic loop from any traction, a more reliably nourished rectal stump, and filling of the presacral space with an intact omentum are the technical innovations being adopted in the current series that could have favorably contributed to control of the anastomotic leakage rates in our series.

Intraoperative damage of the internal anal sphincter and the pelvic floor and the loss of the rectal reservoir function are the main factors that unfavorably affect the functional outcome of LAR.[23] Although occurring in the first year of the postoperative course, alterations of the sphincteric function mostly recovered to normal after this term in all our patients. As previously noted, strict circumferential and caudal clean tissue excision and the cautious management of the internal sphincter might be looked at as the surgical procedures that lead to such satisfactory functional results.

Partial mesorectal excision, tailored on the site of the rectal tumor, has been proposed because this procedure affords lower rates of leakage and better functional results.[15] There is an increasing opinion suggesting the utility of the assessment of local residual disease, the so-called R classification, into staging nomenclature.[1,24,25] Mesorectal NM and NNM were found in the present series to be distal to the primary rectal tumor in 6 patients (11%) and 9 patients (17%), respectively. The strong correlation between the incidence of NNM and other parameters expressing aggressive biological behavior of rectal cancer (Table 2) and the absence of any correlation with parietal tumoral infiltration compare well with previous reports in the literature.[5,7,8] This correlation has been proposed as the rationale to consider the rectum and mesorectum as a single unity to be excised en bloc and intact to improve the staging and curative efficacy of the surgical procedure.[6,12,26] In fact, a perivisceral resection of the rectum or a partial proximal mesorectal excision would have turned into an R1 procedure in the surgery of 24 (45%) and 22 (41%) of our patients, respectively. A careful perirectal soft tissue dissection, while the most determining factor in minimizing pelvic relapse and improving long-term outcome,[27,28] calls into question more extended operations and adjuvant postoperative therapy as overtreating procedures.[3,4,9,12]

In conclusion, as a result of the present work, TME has been confirmed to lower the rate of pelvic recurrence and positively affect the survival after surgical treatment of rectal cancer.[4,6,12,26] Moreover, far from being demanding and time consuming, TME proves to be a straightforward and safe procedure that is effective in reducing perioperative complications.

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ARCHIVES OF INTERNAL MEDICINE

Clinical Prediction of Acute Aortic Dissection

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Background: Clinical criteria for aortic dissection are poorly defined. Thus, 35% of aortic dissections remain unsuspected in vivo, and 99% of suspected cases can be refuted.
Objective: To identify independent predictors of acute aortic dissection and create a prediction model for facilitated estimation of the individual risk of dissection.
Methods: Two hundred fifty patients with acute chest pain, back pain, or both; absence of an established differential diagnosis of the pain syndrome; and clinical suspicion of acute aortic dissection were evaluated for the presence of 26 clinical variables in a prospective, observational study. Multivariate analysis was performed to create a prediction model of aortic dissection.
Results: Aortic pain with immediate onset, a tearing or ripping character, or both; mediastinal widening, aortic widening, or both on chest radiography; and pulse differentials, blood pressure differentials, or both ($P<.001$ for all) were identified as independent predictors of acute aortic dissection. Probability of dissection was low with absence of all 3 variables (7%), intermediate with isolated findings of aortic pain or mediastinal widening (31% and 39%, respectively), and high with isolated pulse or blood pressure differentials or any combination of the 3 variables (≥83%). Accordingly, 4% of all dissections were assigned to the low-probability group, 19% to the intermediate-probability group, and 77% to the high-probability group of aortic dissection.
Conclusions: Assessment of 3 clinical variables permitted identification of 96% of the acute aortic dissections and stratification into high-, intermediate-, and low-probability groupings of disease. With better selection for prompt diagnostic imaging, this prediction model can be used as an aid to improve patient care in aortic dissection. (*2000;160:2977-2982*)

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