An Analysis of Survival and Treatment Failure Following Abdominoperineal and Sphincter-saving Resection in Dukes' B and C Rectal Carcinoma

A Report of the NSABP Clinical Trials

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Abdominoperineal resections for rectal carcinoma are being performed with decreasing frequency in favor of sphincter-saving resections. It remains, however, to be unequivocally demonstrated that sphincter preservation has not resulted in compromised local disease control, disease-free survival, and survival. Accordingly, it is the specific aim of this endeavor to compare local recurrence, disease-free survival, and survival in patients with Dukes' B and C rectal cancer undergoing curative abdominoperineal resection or sphincter-saving resection. For the purpose of this study, 232 patients undergoing abdominoperineal resection and 181 subjected to sphincter-saving resections were available for analysis from an NSABP randomized prospective clinical trial designed to ascertain the efficacy of adjuvant therapy in rectal carcinoma (protocol R-01). The mean time on study was 48 months. Analyses were carried out comparing the two operations according to Dukes' class, the number of positive nodes, and tumor size. The only significant differences in disease-free survival and survival were observed for the cohort characterized by >4 positive nodes and were in favor of patients treated with sphincter-saving resections. A patient undergoing sphincter-saving resection was 0.62 times as likely to sustain a treatment failure as a similar patient undergoing abdominoperineal resection ($p = 0.07$) and 0.49 times as likely to die ($p = 0.02$). The inability to demonstrate an attenuated disease-free survival and survival for patients treated with sphincter-saving resection was in spite of an increased incidence of local recurrence (anastomotic and pelvic) observed for the latter operation when compared to abdominoperineal resection (13% *vs.* 5%). A similar analysis evaluating the length of margins of resection in patients undergoing sphincter-preserving operations indicated that treatment failure and survival were not significantly different in patients whose distal resection margins were <2 cm, 2–2.9 cm, or ≥3 cm. If any trend was observed, it appeared that patients with smaller resection margins had a slightly prolonged survival ($p = 0.10$). This observation was present in spite of the fact that local recurrence as a first site of treatment failure was greater in the group with <2 cm than it was in the ≥3 cm category, 22% *versus* 12%. This increased local recurrence rate in the population with smaller margins was not translated into an increase in overall treatment failure and had absolutely no influence on survival. It is suggested that local recurrence serves as a marker of distant disease. Further, patients undergoing sphincter-saving resections fashioned with mechanical staples fared as well as those subjected to hand-sewn anastomoses. There were no imbalances between the groups for Dukes' class, number of nodes, tumor size, preoperative carcinoembryonic antigen, and type of adjuvant therapy. The data provide the first evidence from a randomized prospective clinical trial that sphincter-saving resection is not associated with an attenuated survivorship or an increased incidence of treatment failure and challenge the prognostic significance of the extent of margins of resection in rectal cancer.

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IT IS A WELL-ESTABLISHED observation that the sphincter-saving resection for rectal cancer is being performed with increasing frequency and that this procedure has made significant inroads into what was once the exclusive domain of the abdominoperineal resection. Although the circular mechanical stapling devices have contributed to the popularity of the sphincter-saving resection, it must be underscored that the retreat from the abdominoperineal resection was motivated by issues exclusive of those related to the anastomotic technique and was underway well before the proliferation of the mechanical stapling implements. Despite the increasing preference for the sphincter-saving resection, it has yet to be unequivocally demonstrated that the use of this procedure has not resulted in attenuated disease control and survivorship.

In order to place the current controversy surrounding the use of the sphincter-saving procedure into appropriate perspective, it is useful to trace the evolution and rationale for the abdominoperineal resection. In 1908 W. Ernest

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Miles described an operation that was noteworthy not for its technical innovation but rather for its conceptual application.[1] It is well established that Miles resurrected a procedure that had been initially described by Czerny in 1884 because of his disenchantment with the standard operative procedure of the day, namely, the perineal method of excision. The abdominoperineal resection represented an eloquent reflection of Miles' biologic understanding of the behavior and dissemination of rectal cancer and was formulated following an analysis of the pelvic distribution of locally disseminated rectal cancer in postmortem examinations and in patients with locally advanced inoperable disease. Based on these observations, Miles concluded that there were three principal lymphatic zones of tumor dissemination that had to be addressed if the cancer was to be successfully extirpated: (1) the zone of downward spread, consisting of the perianal skin, ischiorectal fat, and the external sphincter muscles; (2) the lateral zone of spread, comprised of the lymphatic network between and including the levator ani muscles and pelvic fascia as well as the pelvic peritoneum; and (3) the zone of upward spread characterized by the retro-rectal glands, pelvic mesocolon, the paracolic glands, the glands at the bifurcation of the left common iliac artery, and the median lumbar glands. It was Miles' contention that this latter zone of upward spread represented the principal route of tumor dissemination because within this zone "secondary deposits were *always* present, visible to the naked eye or discernable by the microscope."[2] Although the perineal method of excision adequately addressed the downward and lateral zone of spread, it entirely ignored the putatively most important zone of upward spread. With the popularization of the abdominoperineal resection, Miles for the first time applied the principles of *en bloc* dissection to carcinoma of the rectum and brought the operation into line with those that had been advocated for carcinoma of the breast and carcinoma of the cervix. It is of interest that Miles admonished his colleagues that "it is just as important to remove the whole of the structure at an operation for cancer of the rectum as it is to clear the axilla thoroughly during an operation for cancer of the breast,"[2] a feat that could only be accomplished with the addition of an abdominal dissection to the perineal excision. Based on these principles, over the next 2 decades the abdominoperineal resection rapidly supplanted (with few notable exceptions)[3] the perineal method of excision. With the widespread application of the abdominal approach to carcinoma of the rectum, it is not surprising that attempts were eventually made to restore bowel continuity by eliminating the perineal component of the operation. In 1930 Dixon introduced the anterior resection and by the time of his address to the American Surgical Association in 1948 had applied the procedure to 523 patients with seemingly remarkable success.[4] The anterior resection clearly violated the hypotheses that were germane to the evolution of the abdominoperineal resection. Although the abandonment of the perineal component of the operation did not necessarily alter the approach to the zone of upward spread, significant compromise occurred in addressing the zones of lateral and downward spread, thus challenging the very basis on which the abdominoperineal resection had evolved. Moreover, efforts to preserve the anal sphincter were often performed at the expense of the traditional 5 cm minimal distal resection margin considered optimum in the control of local recurrence of disease.

Despite numerous retrospective and anecdotal analyses attesting to the safety of the sphincter-saving resection, the contention that the failure to widely excise the perineum is associated with attenuated survival and increased incidence of recurrence has yet to be definitively assuaged. The studies cited in the literature that have attempted to compare abdominoperineal resection with sphincter-saving procedures are all derived from retrospective studies in which the historical control group was not infrequently obtained from a nonconcomitant data set.[5-18] Moreover, little effort was made to assure the comparability of the two groups in question with respect to the distribution of prognostic discriminants such as Dukes' class and the number of positive nodes.

In an effort to resolve some of the biologic and practical disputations surrounding the efficacy of sphincter-saving operations, it was considered appropriate to evaluate the data from the randomized prospective rectal cancer trial of the National Surgical Adjuvant Project for Breast and Bowel Cancer (NSABP). This study was primarily designed to evaluate the utility of adjuvant chemotherapy and radiotherapy following curative resection for Dukes' B and C rectal cancer. Although the original specific aims of the study were not formulated to compare treatment failure and survival in patients treated with sphincter-saving resection and abdominoperineal resection, nonetheless a large patient cohort was available in whom the two operations were performed without specific protocol-determined selection bias. Despite this limitation, data were derived from patients treated with either procedure who were entered in a randomized prospective manner albeit not specifically for the end points considered in this analysis. Accordingly, the principal specific aim of the study described herein is to compare local recurrence, disease-free survival, and survival in patients undergoing abdominoperineal resection or sphincter-saving operation following curative resection for Dukes' B and C rectal cancer. Further, it is the intent of this endeavor to ascertain the significance of the length of distal margins of resection in those patients in whom the sphincter was spared.

Materials and Methods

Data for this analysis were derived from NSABP protocol R-01, a randomized prospective clinical trial de-

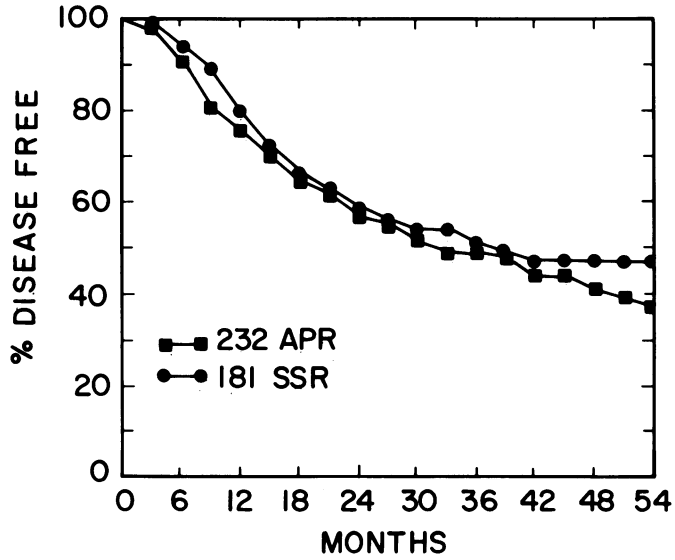

FIG. 1. Disease-free survival of Dukes' B and C rectal cancer patients treated with abdominoperineal resection (APR) and sphincter-saving resection (SSR).

signed to determine the utility of adjuvant therapy in patients with carcinoma of the rectum. Protocol design and patient accession have been described in greater detail elsewhere.[19] The population employed in this study consisted of patients with documented Dukes' B and C rectal cancer who were entered following protocol initiation in November 1977. Randomization was effected to three therapeutic categories: (1) no further treatment following curative resection, (2) postoperative radiotherapy, or (3) postoperative chemotherapy consisting of 5-fluorouracil, MeCCNU (semustine), and vincristine.

Reference to Dukes' classification was according to the classical criteria described in 1932 for carcinoma of the rectum.[20] Dukes' B lesions were characterized by extension of tumor through the muscularis propria into the perirectal adipose tissue without regional lymph node metastases; Dukes' C tumors were exemplified by regional node metastases with any depth of tumor penetration.

This analysis does not include tumors that, because of metastatic disease or contiguous involvement, extended beyond the scope of curative operative resection. A rectal tumor was defined by protocol as any lesion that required the opening of the pelvic peritoneum to define the distal extent of the tumor. Patients with rectal tumors were treated either with anterior resection or abdominoperineal resection, with the operative conduct determined by the protocol.

For the purpose of this analysis, 232 patients undergoing abdominoperineal resection and 181 patients in whom the sphincter was preserved were available for assessment; of the latter group, 82 anastomoses were mechanically stapled and 99 were hand-sewn. The average time on study was 48 months. The length of the distal resection margin was reported by the institution pathologist as was the maximum tumor diameter.

Two varieties of statistical analyses were carried out. In the first instance, use was made of the Mantel–Haenszel statistic in order to test the differences in disease-free survival between two or more groups. In general, when the Mantel–Haenszel statistic is discussed, reference is made to the two group test, and whenever a p value is provided, it is two-sided. Another measure that was used, and may be as important as the p value when dealing with prognostic factors, was the relative risk of treatment failure. Whenever the Mantel–Haenszel statistic was used for comparison of two groups, the observed and expected number of treatment failures were computed. Letting 01 (E1) and 02 (E2) be the number of observed (expected) failures in groups 1 and 2, respectively, the relative risk of group 2 to group 1 was defined by (02/E2)/(01/E1). If this value was equal to one, the two groups had "equivalent" prognoses, whereas a relative risk of greater than one indicated that the prognosis of group 2 was worse than that of group 1, and a relative risk of less than one indicated that the prognosis of group 2 was better than that of group 1. If the relative risk was two, for example, a patient from group 2 was roughly twice as likely to fail as a patient from group 1 (hence the expression relative risk of group 2 to group 1).

Second, the Mantel–Haenszel test also may be used to compare the risk of dying as a result of a particular discriminant while controlling for imbalances due to confounding variables (such as the number of positive nodes). This procedure enables the testing of the equivalence of treatments while taking into account the effects of other covariates. In the analyses presented, correction for Dukes' class, nodal imbalances, and adjuvant treatment has been carried out.[21,22]

Results

Disease-free Survival and Survival in Patients Treated with Abdominoperineal Resection or Sphincter-saving Procedures

Examination of disease-free survival and survival for the combined Dukes' B and C rectal population (all patients) disclosed that there was no significant disadvantage for the use of sphincter-preserving operations. Patients treated with the latter procedure were 0.82 times as likely to die or fail as those in whom the sphincter and perineum were sacrificed (Table 1, Fig. 1). An attenuated disease-free survival and survival for patients treated with the sphincter-preserving operation could not be demonstrated despite an increased incidence of local recurrence as a first site of treatment failure (anastomotic and pelvic) observed for the latter operation when compared to the ab-

TABLE 1. *Treatment Failure and Survival SSR* Versus *APR*

	APR			SSR			Relative Risk of Failure		Relative Risk of Death	
	No.	Failed	Died	No.	Failed	Died	SSR *vs.* APR	p	SSR *vs.* APR	p
All patients	232	103	79	181	70	52	0.82	NS	0.82	NS
Dukes' B	86	26	15	60	13	8	0.89	NS	1.14	NS
Dukes' C	146	77	64	121	57	44	0.81	NS	0.76	NS
1–4 nodes	78	32	25	69	28	22	0.90	NS	0.96	NS
>4 nodes	51	34	29	41	21	15	0.62	.07	0.49	0.02
Tumor diameter										
<6 CM	124	48	35	126	46	31	1.07	NS	1.05	NS
≥6 CM	77	36	28	37	14	12	0.71	NS	0.81	NS

APR = abdominoperineal resection; SSR = sphincter-saving resection.

dominoperineal resection: 13% *versus* 5%, p = 0.0002. Contrariwise, distant disease as a first site of treatment failure was significantly reduced in patients with sphincter-saving resections when compared to those receiving abdominoperineal resections: 24% *versus* 39%.

Although the data were adjusted for the effects of adjuvant treatment, it was considered worthwhile to examine the results for the control group alone. When the same analysis was therefore carried out for the group randomized to receive no further treatment following curative resection, no significant differences were observed between the two operations with respect to treatment failure and survival; patients in whom bowel continuity was restored were at 0.77 times the relative risk of failing and 0.97 times as likely to die as individuals treated with the Miles operation. Although the above-described analyses were adjusted for imbalances in Dukes' class and the number of positive nodes, the data were separately examined for patients with Dukes' B and C lesions (Fig. 2) as well as those with 1–4 or >4 metastatic lymph nodes (Fig. 3). No significant differences were noted in either disease-free survival or survival when the results were analyzed according to Dukes' class (Table 1, Fig. 2). For example, a patient with a Dukes' C tumor (adjusted for the number of positive nodes) was 0.81 times as likely to fail and 0.76 times as likely to die if treated with a sphincter-saving operation as compared with an abdominoperineal resection. The only significant differences in disease-free survival and survival were observed for the cohort characterized by >4 positive nodes and were in favor of patients treated with sphincter-preserving operations. A patient treated with the latter procedure was 0.62 times as likely to sustain a treatment failure as a similar patient undergoing an abdominoperineal resection (p = 0.07) and 0.49 times as likely to die (p = 0.02, Fig. 3).

Comparison of the two operative procedures was then carried out according to the maximum diameter of the tumor as well as tumor volume in order to address the contention that larger tumors are more effectively managed by abdominoperineal resection. No significant differences in disease-free survival and survival were in evidence when the two procedures were examined in patients with tumors of maximum diameter of <6 cm or ≥6 cm. Curiously enough, a patient with a tumor ≥6 cm was only

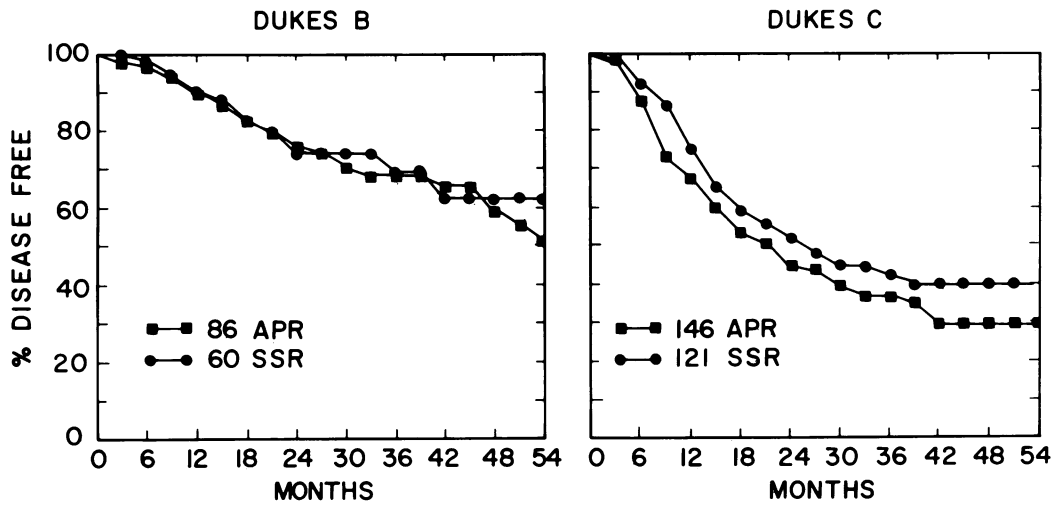

FIG. 2. Disease-free survival according to Dukes' class for rectal cancer patients treated with abdominoperineal resection (APR) and sphincter-saving resection (SSR).

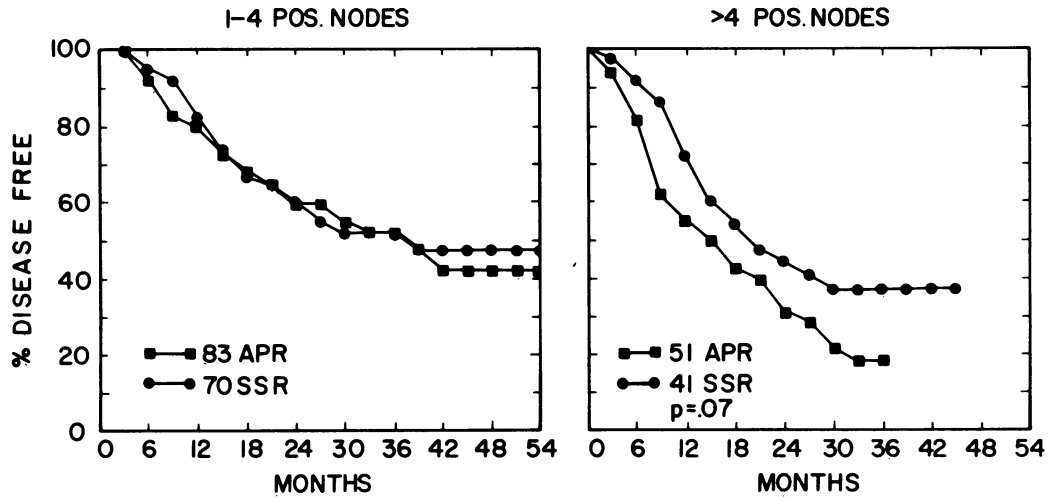

FIG. 3. Disease-free survival according to the number of positive nodes for rectal cancer patients treated with abdominoperineal resection (APR) and sphincter-saving resection (SSR).

0.71 times as likely to fail and 0.81 times as likely to die when treated with a sphincter-preserving operation as was a similar patient treated with abdominoperineal resection (Table 1, Fig. 4).

A similar analysis conducted for patients with tumor volumes <50 cc and ≥50 cc (product of three perpendicular diameters) provided similar results (data not shown). The analyses addressing tumor diameter and volume were adjusted for protocol treatment, Dukes' class, and the number of positive nodes.

It should be noted that there were no significant imbalances observed in the two operative procedures relative to age, preoperative carcinoembryonic antigen, or the proportion of lumen encirclement by tumor.

Disease-free Survival and Survival According to Length of Distal Resection Margins in Patients Treated with Sphincter-saving Resections

Evaluations were carried out according to three groupings characterizing the distal margin of resection; <2 cm, 2–2.9 cm, and ≥3 cm. Analysis of disease-free survival and survival according to these categories failed to indicate significant differences in overall treatment failure and survival. Patients with smaller resection margins appeared to fare as well as those with more generous lengths of tumor clearance (Table 2, Fig. 5). For example, a patient with a distal margin of <2 cm was 0.88 times as likely to fail and 0.57 times as likely to die as a patient with a distal margin of ≥3 cm. If any trend was observed, it appeared that patients with smaller resection margins had a slightly prolonged survival (p = 0.10). This observation was present in spite of the fact that local recurrence as a first site of treatment failure was greater in the group with <2 cm than it was in the ≥3 cm category, 22% *versus* 12%. This increased local recurrence rate in the population with smaller margins was not translated into an increase in overall treatment failure and had absolutely no influence on survival.

Although these analyses were conducted adjusting for Dukes' class and the number of positive nodes, further

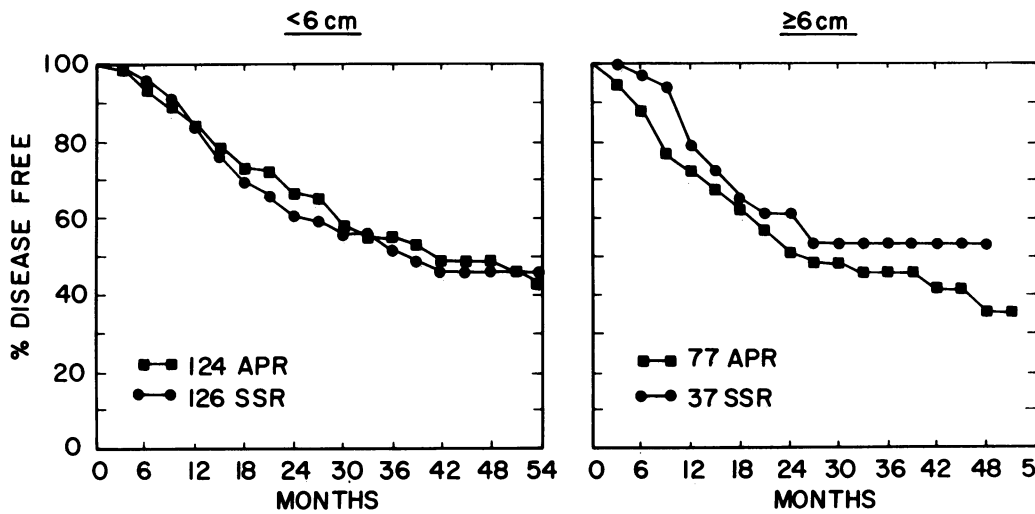

FIG. 4. Disease-free survival according to maximum tumor diameter for rectal cancer patients treated with abdominoperineal resection (APR) and sphincter-saving resection (SSR).

TABLE 2. *Treatment Failure and Survival According to Margins of Resection*

cm	No.	Failed	Died	Relative Risk of Failure *vs.* >3 cm	p	Relative Risk of Death *vs.* >3 cm	p
All patients							
<2	45	17	11	0.88	NS	0.57	0.10
2–2.9	56	21	14	0.81	NS	0.63	NS
≥3	67	26	22	1.00	—	1.00	—
Dukes' C							
<2	31	11	8	0.51	0.07	0.44	0.04
2–2.9	42	19	13	0.82	NS	0.62	0.17
≥3	41	21	18	1.00	—	1.00	—

efforts addressed the significance of resection margins according to Dukes' class. There were too few patients in the Dukes' B category to allow for meaningful analysis; however, examination of the data for patients with Dukes' C lesions further underscored the trends noted for the combined population. Whereas the survival advantage noted in the <2 cm category only approached significance in the overall analysis, in the Dukes' C category a resection margin of <2 cm was associated with a 0.44-fold risk of death when compared to the ≥3 cm group ($p = 0.04$). The data were again adjusted for the number of positive nodes.

Discussion

The challenge to the abdominoperineal resection, although principally motivated by the desire to avoid permanent colostomy, has far reaching biological consequences. If it can be unequivocally demonstrated that sphincter-saving procedures are the equal of those in which the perineum and anus are sacrificed, the hypotheses on which the abdominoperineal resection was evolved must be re-evaluated. The assault on the basis for the Miles operation, although not a new phenomenon, has gained momentum over the past decade. Efforts to discredit the Miles procedure (in those instances when restoration of bowel continuity is technically feasible) have taken on various forms both direct and indirect. These efforts have been oriented toward anatomic and technical themes rather than on issues related to the biology of tumor dissemination and metastasis. The indirect methods have focused on analyzing and mapping the anatomic distribution of local pelvic tumor encroachment and contrasting the findings with those initially put forward by Miles and his colleagues. There are ample instances cited in the literature to indicate that some of the contentions on which the abdominoperineal resection was based are subject to serious dispute. The conviction that the "zone of distal spread" is of clinical relevance has had a profound influence on the conduct of operations in carcinoma of the rectum and has been responsible for the arbitrary selection of 5 cm as the minimum requirement for the length of the distal resection margin. Review of the literature relative to this subject will adumbrate numerous studies in which the occurrence of distal intramural and retrograde lymphatic spread (below the level of the tumor) is an exceedingly rare phenomenon and when it does occur is associated with an ominous prognosis, regardless of the operative procedure selected (reviewed in ref. 17). In no instance has an effort been made to determine whether distal intramural involvement or retrograde lymphatic permeation are independent prognostic discriminants or are simply associated with advanced Dukes' class or disease that has already metastasized. Similar challenges have been advanced with respect to the significance of the "zone of lateral spread." Once again studies may be cited in which the presence of lateral lymphatic involvement has been shown to be an uncommon finding and when present serves as a harbinger of disseminated disease. Not even the pivotal "zone of upward spread" has escaped the in-

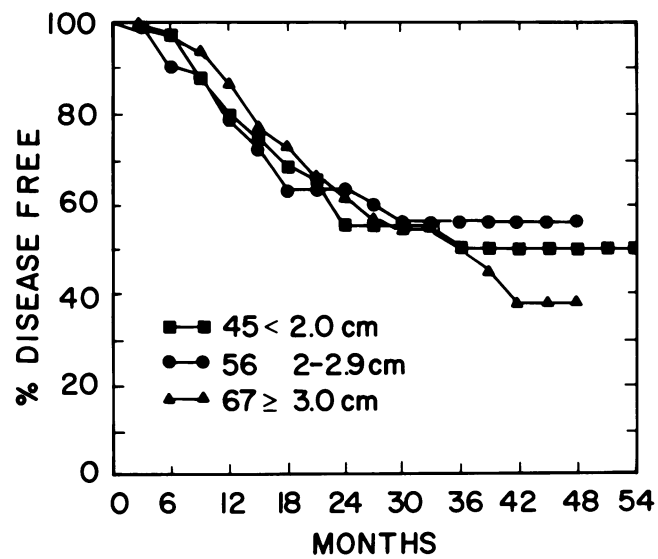

FIG. 5. Disease-free survival according to the length of distal resection margins in rectal cancer patients (Dukes' B and C) treated with sphincter-saving resections.

veterate gibes of the anatomic critic. Gabriel and colleagues challenged the significance of the paracolic glands along the mesenteric border of the pelvic colon.[23] Lest the subtlety of this challenge be lost, all doubt was removed by the following statement: "Miles states that the paracolic glands situated along the mesenteric border of the pelvic colon are often the seat of metastatic deposits. This has not been our experience; in fact we have found metastases in the paracolic glands only in one case [of 100 examined]." Further, the polemics surrounding the incidence and significance of nodes located in the 4 cm region between the origin of the left colic artery and the origin of the inferior mesenteric artery are well known and need not be further belabored.[1-2,24-26]

It is important that these indirect methods of challenge of the rationale for the abdominoperineal resection be placed into appropriate perspective. The fact that one can successfully dispute the basis on which an operative procedure was evolved does not necessarily imply that the operation is without merit. Although an operation may have evolved based on an erroneous premise, it may still represent the optimum method of therapy. Accordingly, the ultimate test for the utility of the abdominoperineal resection must be obtained from a well-controlled trial comparing this procedure with those restoring bowel continuity. Here too there have been instances in which the two operations have been assessed, and, for the most part, no striking differences have been observed with respect to survival.[5-18] Without exception, these analyses were derived from nonrandomized retrospective studies lacking a suitable concomitant control. Moreover, the failure to adjust for possible maldistribution of important prognostic indices may have resulted in imbalances that have a major confounding influence on final outcome.[27] The same criticisms may be directed towards those studies that have evaluated distal resection margins as prognostic discriminants in anterior resections.[6,28-32]

The results presented herein represent the first obtained from a prospective clinical trial. The data are unequivocal in indicating that there was no demonstrable disadvantage for the use of sphincter-saving resections utilizing disease-free survival and survival as end points. This conclusion was apparent in all patient subsets examined as characterized by Dukes' class and the number of positive nodes. The significant survival advantage observed in patients treated with sphincter-saving resection with >4 positive regional nodes remains enigmatic. It would be in precisely this patient population that one might anticipate a salutary effect for the abdominoperineal resection were Miles' hypotheses correct. In patients with many positive nodes, one can argue that there is a greater likelihood of leaving nodal disease behind if the zones of lateral and downward spread are not adequately extirpated. The fact that no such disadvantage is noted for sphincter preservation in the >4 nodal cohort represents a strong challenge to the biologic and therapeutic bases for the abdominoperineal resection.

Tumor size and volume have often been cited as useful discriminants in selecting the type of operative procedure to be performed. It has been argued that optimum disease control in larger tumors will be more readily effected by including the perineal component of the operation. The results obtained in this study do not support this contention. Tumors with maximum diameters of ≥6 cm or volumes ≥ 50 cc did not demonstrate an increased treatment failure rate when treated by sphincter-saving resection as compared to similar tumors treated by abdominoperineal resection. The findings also support the conclusions from a previous NSABP analysis in which it was demonstrated that tumor size was not a major prognostic discriminant in Dukes' B and C adenocarcinoma.[19,33]

It has been argued that variations in the height of the tumor for the two treatment options can introduce a source of bias. Measurements of the height of rectal tumors were not presented in this analysis because the large variability associated with the methods employed in the multi-institutional setting makes this information cumbersome to standardize. Of far greater importance is the consideration of whether a comparison of the two operations based on height of tumor from the dentate line represents a valid analysis. The majority of tumors for both abdominoperineal resection as well as sphincter-saving procedures falls within the "mid rectum." This leaves small sample sizes at either extreme, *i.e.,* the upper rectum or lower rectum (distal 5 cm). Accordingly, an analysis based on tumor height may have merit when postoperative misadventures are assessed, but it is to be condemned when disease-free survival and survival are measured, unless extremely large populations are available. Accordingly, this analysis does not address the specific situation of rectal resections requiring coloanal anastomoses.

Perhaps the most intriguing challenge to the therapeutic rationale for the abdominoperineal resection is forthcoming from the analysis of length of distal margins of resection. Protocol R-01 provided an opportunity to address the postulate that attenuated resection margins result in an increased incidence of local recurrence and decreased disease-free survival and survival. The data clearly do not support this hypothesis. Patients with resection margins of <2 cm were not at a disadvantage when compared with patients with more generous margins of clearance. Although the <2 cm margin group demonstrated an increased incidence of local tumor recurrence as the first site of treatment failure, there was a complementary decrease in distant disease as the first site of treatment failure, indicating that local recurrence probably serves as a marker of distant disease. Further, the increased incidence of local failure in this group was not translated to a de-

creased survivorship; if anything, patients with shorter resection margins had a better survival that reached statistical significance for the Dukes' C cohort. Parenthetically, it might be added that the type of anastomosis performed, *i.e.*, hand-sewn or stapled, had little influence on local or distant recurrent disease. The average margin of distal clearance was identical in the hand-sewn and stapled patient groups.[34]

It may therefore be concluded that the data provide the first evidence from a randomized prospective trial that sphincter-saving resections are not associated with attenuated survivorship in those patients in whom such an operation is technically feasible. Further, the prognostic significance of the extent of margins of resection is refuted. The findings raise serious questions as to the validity of the biologic and therapeutic rationale on which the abdominoperineal resection was based. There are unmistakable parallels between the evolution of the operative strategy of carcinoma of the rectum and that of breast cancer. One cannot help but wonder whether Miles' efforts to bring his operation in line with the *en bloc* operations of his contemporaries will not meet the same fate as the radical mastectomy.

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Appendix

Institution	Principal Investigator
Albany Regional Cancer Center, NY	Thomas Cunningham
Albert Einstein College of Medicine, NY	Herbert Volk
Albert Einstein Medical Center, Phila., PA	Stanley Levick/ Ajit Desai
Allentown Hospital, PA	David Prager
Baptist Memorial Hospital, Pensacola, FL	Allan Patton
Berkshire Medical Center, Pittsfield, MA	Jesse Spector/ Harvey Zimbler
Billings Interhospital Oncology Project, MT	David Myers
Boston University	Merrill Feldman
Bowman Gray School of Medicine, NC	John Michael Sterchi
Brentwood Hospital, Warrensville Hts., OH	B. L. Horvat
Bryn Mawr Hospital, PA	Thomas G. Frazier
Camden-Clark Memorial Hospital, WV	Nikunj Shah
City of Hope Medical Center, Duarte, CA	Jose J. Terz
Denver General Hospital	George Moore
Downstate Medical Center, SUNY	Bernard Gardner
Ellis Fischel State Cancer Hospital, MO	William Kraybill
Geisinger Medical Center, Danville, PA	James Evans
Good Samaritan Hospital, Lexington, KY	William Meeker
Gulf Coast Community Hospital, Panama City	William Gregory Bruce
Harbor General Hospital, Torrance, CA	David State/ M. Michael Shabot
Highland Hospital, Rochester, NY	Sidney Sobel
Hotel-Dieu, Montreal	Andre Robidoux
Hotel-Dieu, Quebec City	Louis Dionne
Jewish General Hospital, Montreal	Richard Margolese
Kaiser Permanente, Portland, OR	Andrew Glass
Kaiser Permanente, San Diego, CA	Thomas Campbell
Letterman Army Medical Center, CA	David Gandara
Louisiana State University, New Orleans, LA	Isidore Cohn/ Robert Beazley
Louisiana State University, Shreveport, LA	Don M. Morris
Manitoba Cancer Foundation	David Bowman
Marshfield Clinic, WI	James L. Hoehn
Medical College of Virginia	Walter Lawrence
Medical College of Wisconsin	William Donegan
Memorial Cancer Research Foundation, CA	David Plotkin
Michael Reese Hospital, Chicago, IL	Richard Desser
Michigan State University, East Lansing, MI	Leif Suhrland
Montefiore Hospital ≤ Medical Center, NY	Richard Rosen
Montreal General Hospital	John MacFarlane
Mount Sinai Hospital, Milwaukee, WI	Jules Lodish
Mount Sinai Medical Center, Cleveland, OH	Richard Bornstein/ Jeffrey L. Ponsky
Naval Regional Medical Center, Oakland, CA	Michael A. Crucitt
Naval Regional Medical Center, San Diego, CA	Jim Guzik
Pennsylvania Hospital	Harvey Lerner
Royal Victoria Hospital, Montreal	Henry Shibata
Rush Presbyterian–St. Luke's Medical Center, IL	Janet Wolter/ Steven Economou
South Nassau Communities Hospital, NY	Nicholas LiCalzi
St. Joseph Hospital, Lancaster, PA	H. P. DeGreen
St. Luc Hospital, Montreal	Roger Poisson/ Sandra Legault-Poisson
St. Luke's Hospital, Kansas City	Paul Koontz
St. Mary's Hospital, Grand Rapids, MI	Andre Jubert
St. Michael's Hospital, Toronto	Leon Mahoney
St. Vincent's Hospital, IN	John Cavins
St. Vincent's Hospital, NY	Thomas Nealon
Tom Baker Cancer Centre, Calgary	L. Martin Jerry
Trumbull Memorial Hospital, Warren, OH	Jerome Stanislaw
Tulane University, New Orleans	Carl Sutherland
University of California, San Diego	Yosef Pilch
University of Florida, JHEP	Neil Abramson
University of Hawaii	Noboru Oishi/ Robert Oishi
University of Iowa	Peter Jochimsen
University of Louisville	Joseph Allegra
University of Maryland	E. George Elias
University of Massachusetts, Worchester, MA	Mary Costanza/ Michael Wertheimer
University of North Carolina	Robert Capizzi
University of Pittsburgh	Bernard Fisher
University of Texas, San Antonio, TX	A. B. Cruz/ J. Bradley Aust
University of Vermont	Roger Foster
VA Medical Center, Boston, MA	Waun Hong
Valley Hospital, Ridgewood, NY	Hugh Auchincloss
Washington Regional Medical Center, AR	James H. Bledsoe
West Suburban Hospital, Oak Park, IL	Everett Nicholas
West Virginia University, Morgantown, WV	Alvin Watne
White Memorial Medical Center, Los Angeles, CA	Matthew Tan
Wilmington Medical Center, DE	Robert Frelick
Wuesthoff Memorial Hospital, Rockledge, FL	Edward W. Knight

Discussion

DR. JEROME J. DECOSSE (New York, New York): I have two questions, Dr. Wolmark, regarding your interesting presentation. First, have you demonstrated differences in abdominal-perineal resection *versus* sphincter saving resection only for that subset between 5 and 12 cm from the anal verge, for that is all that really counts in making a comparison?

Second, would you tell us what that distal margin means? Is that a margin in the operating room, is it a margin with the specimen in your hand, or is it a margin with the specimen in formalin?

DR. PAUL TARTTER (New York): Some years ago I looked at differences in survival between patients who had low anterior resections and those who had abdominal-perineal resections, and I found results very similar to what we have heard today. The problem was that, after controlling for the distance from the anal verge, I found that the higher the lesion was in the rectum, the better the prognosis. I went back to the literature, and several other examiners had found the same thing. I wonder if Dr. Wolmark has looked at distance from the anal verge as a prognostic factor in these patients.

DR. WANEBO (Charlottesville, Virginia): Dr. Wolmark, I have one question, and it concerns the problem about selection. The selection of surgical procedure APR *versus* anterior resection was not randomized, and one wonders if there could still be some disparity. That is, the larger lesions might have been more likely handled by an APR by the surgeons