Radical Abdominopelvic Lymphadenectomy: Historic Perspective and Current Role in the Surgical Management of Rectal Cancer

Jeffrey R. Harnsberger, M.D., Anthony M. Vernava III, M.D., Walter E. Longo, M.D.

From The Department of Surgery, Section of Colon and Rectal Surgery, St. Louis University School of Medicine, St. Louis, Missouri

Radical abdominopelvic lymphadenectomy for rectal cancer is based on the tenet that removal of all potentially involved lymphatic tissue will yield a lower rate of locoregional failure and improve survival. At centers with extensive experience with the procedure, the operating time is only modestly prolonged compared with conventional resection. Blood loss and postoperative hospitalization are not significantly increased. Urinary dysfunction and impotence associated with radical abdominopelvic lymphadenectomy (as high as 80 percent and 76 percent, respectively, in recent series) have been major deterrents to its more routine application. Preservation of the hypogastric plexus and even selective preservation of a unilateral S4 nerve root have been shown to reduce the occurrence of genitourinary complications. Improved five-year survival of 68 percent and local recurrence rates of 5 to 20 percent for TNM Stage III cancers have been achieved with radical abdominopelvic lymphadenectomy. These results compare favorably with recent trials of adjuvant chemoradiation after conventional resection in stage-matched patients. The rationale, evolution, and application of radical abdominopelvic lymphadenectomy to the surgical management of rectal cancer are critically examined. The potential benefits of radical abdominopelvic lymphadenectomy, which have been demonstrated in nonrandomized trials, should be evaluated in a prospective and properly randomized study to clearly establish or refute its efficacy. [Key words: Rectal cancer; Radical abdominopelvic lymphadenectomy; Outcome]

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Address reprint requests to Dr. Vernava: Chief, Section of Colon and Rectal Surgery, Department of Surgery, St. Louis University School of Medicine, 3635 Vista at Grand Boulevard, P.O. Box 15250, St. Louis, Missouri 63110–0159.

Carcinoma of the rectum affects over 45,000 persons in the United States annually.[1] Despite intensive basic research, clinical investigation, and multimodality adjuvant therapy, mortality rates for rectal cancer have not appreciably improved over the past 50 years.[1, 2] Nonetheless, survival and recurrence for surgically treated rectal cancer have not been adversely affected by either shortened surgical margins[3–7] or the widespread use of sphincter-preserving operations.[3, 4, 6, 8–14] Although these developments have broadened the spectrum of acceptable surgical approaches to carcinoma of the rectum, and presumably improved patient lifestyle, they have not been accompanied by survival improvement.[15–19] The optimal surgical management of rectal cancer remains an area of investigation.

In 1908, Miles[20] championed the concept of improving survival from rectal cancer by excising the rectum, with its lymphatic drainage, up to the level of the ascending branch of the left colic artery. Moynihan[21] extended this concept and recommended removal of even more proximal lymphatics by dividing the inferior mesenteric artery at the level of the aorta. Based on these early reports, interest gradually developed regarding the possibility of improving survival by a more radical *en bloc* excision of lymphatics draining the rectum. Survival benefit for radical abdominopelvic lymphadenectomy (RAPL) has been difficult to definitively establish and has been attended by significantly higher morbidity and mortality compared

with less extensive resections for rectal cancer. However, several recent reports suggest that more aggressive resection of the pararectal lymphatics is associated with improved survival.[22-26] Our review examines the anatomic and clinical information from which the concept of RAPL evolved and attempts to define its role in the current management of carcinoma of the rectum.

RATIONALE FOR RAPL

It is likely that locoregional failure, delayed development of metastatic disease, and poor long-term survival from rectal cancer are, at least in part, attributable to the presence of occult residual tumor in pararectal and para-aortic lymphatics which drain the primary rectal cancer. Radical, *en bloc*, surgical excision of potentially involved lymphatic tissue may yield improvement in locoregional control of the disease and, ultimately, result in improved overall survival. The foundation upon which these tenets are based lies in an understanding of the normal lymphatic drainage of the rectum and the precise patterns of involvement of these lymphatics by rectal cancer. This information provides the anatomic basis for RAPL and is reviewed.

NORMAL LYMPHATIC DRAINAGE OF THE RECTUM

Before examination of the patterns of lymph node metastases in rectal cancer, the normal lymphatic drainage of the proximal, middle, and lower rectum should be understood (Fig. 1). The upper one-third of the rectum is drained chiefly by lymphatics which course along the superior rectal artery (SRA) and inferior mesenteric artery (IMA) to the para-aortic nodes. Lymphatic drainage along the inferior mesenteric vein to the paraportal lymphatics occurs to a lesser extent. Two systems of lymphatic drainage exist for the lower two-thirds of the rectum. Cephalad drainage occurs along the SRA and IMA. Lateral lymphatic drainage occurs along the middle rectal vessels to the internal and common iliac nodes. Recent studies using lymphoscintigraphy fail to demonstrate communication between inferior mesenteric and internal iliac lymphatics.[27] The low rectum, above the dentate line, drains *via* the middle and inferior rectal lymphatics to the internal iliac nodes. Upward spread may also occur along the superior rectal and inferior mesenteric lymphatics. Below the dentate line,

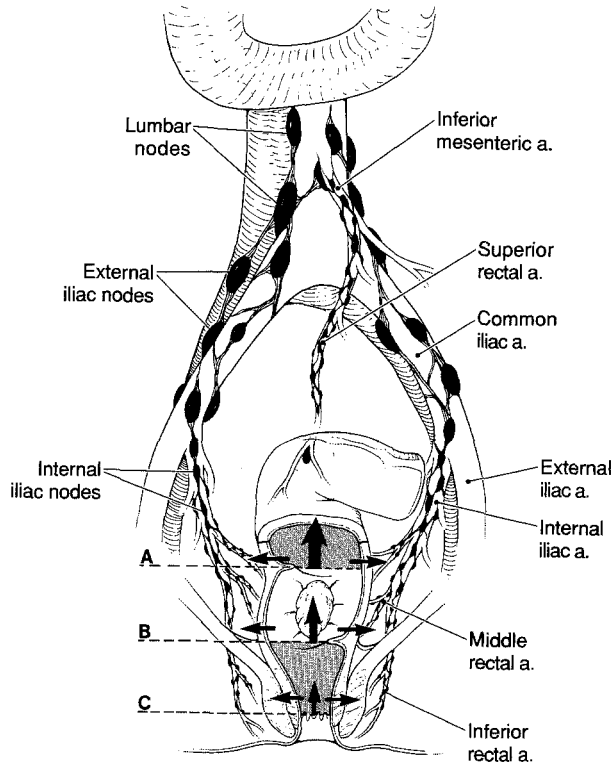

Figure 1. Normal lymphatic drainage of the rectum. A. *Upper third of rectum:* Lymphatic drainage mainly occurs along the SRA and IMA to the para-aortic nodes. Lymphatic drainage can also occur along the inferior mesenteric vein (IMV) to the paraportal lymphatics. B. *Middle third of rectum:* Cephalad lymphatic drainage occurs along the SRA and IMA. Lateral lymphatic drainage occurs along the middle rectal vessels to the internal and common iliac nodes. C. *Lower third of rectum:* Lymphatic drainage is predominantly lateral and occurs along the middle and inferior rectal vessels to the internal iliac nodes. Cephalad drainage can also occur along the SRA and IMA.

anal canal lymphatic drainage occurs along inferior rectal lymphatics to the superficial inguinal nodes. These pathways are illustrated in Figure 1. Lymphangiography has also clearly shown rectal lymphatic drainage to the broad ligament and reproductive organs in females.[28]

PATTERNS OF LYMPHATIC SPREAD FROM RECTAL CANCER

Detailed anatomic studies have examined the patterns of lymphatic spread from rectal cancer and provide the theoretic rationale for attempting to improve survival with radical *en bloc* pelvic lymphadenectomy. Gabriel *et al.*[29] performed detailed dissection and anatomic mapping of 100 cases of rectal cancer. Metastases to lymph nodes were noted in 62 percent of specimens. There was an

orderly progression of metastases to perirectal, superior rectal, and then inferior mesenteric lymph nodes. In only one case was metastatic disease present at the proximal mesenteric ligature when there was no metastatic involvement of the intervening lymphatics. Other reports, however, indicate that such discontinuous lymphatic metastasis occurs more frequently. Discontinuous patterns of nodal metastases were noted in 6 of 51 (12 percent) cases in a report by Wood and Wilkie,[30] and in 7 of the 41 specimens (17 percent) examined by Grinnell.[31] In Grinnell's[31] series, over half of the metastatic nodes were within 3 cm of the primary tumor. It is apparent from these studies that wider lymphatic resection would be necessary to surgically excise all involved and potentially involved regional lymphatics.

Retrograde or downward lymphatic spread of rectal cancer rarely occurs. As emphasized by Gilchrist,[32] retrograde metastasis probably occurs as an embolic event when the primary lymphatic drainage routes are blocked by disease. Retrograde metastasis was observed in only 1 of over 40 patients in early reports by Grinnell,[31] Gilchrist and David,[33] Gabriel *et al.*,[29] and Coller *et al.*[34] Subsequent studies by Grinnell[35] demonstrated somewhat more frequent caudad metastases in 5 of 118 rectal cancer specimens. Gilchrist and David[36] reported similar findings in 7 of 153 cases. These authors[35,36] recommended routine wide mesenteric resection.

A discussion of the merits of RAPL centers around the lateral spread of rectal cancer along the middle hemorrhoidal vessels. Early anatomic studies reported that lateral spread rarely occurred. Wood and Wilkie[30] could not demonstrate lateral lymphatic spread in 51 specimens. Grinnell[31] found 1 such instance in 41 (2 percent) cases. Gilchrist and David[33] noted lateral metastasis in only 4 of 47 (9 percent) cases. Subsequent studies, however, demonstrated higher rates of lateral lymphatic spread. Coller *et al.*[34] reported superior and lateral lymph node metastases in 6 of 11 cases (54.5 percent) of low rectal cancers. Hojo *et al.*[37] identified lateral lymph nodal spread in 23 percent of 423 patients. Mascagni *et al.*[38] reported a 20 percent lateral lymph node involvement in their most recent review. Sauer and Bacon[39] studied *in vivo* lymphatic drainage patterns by injecting Evans blue dye into the low rectal mucosa of preoperative patients. They clearly demonstrated lymphatic drainage along the middle rectal vessels within the lateral ligaments. This data led to revision of the early descriptions of lateral rectal lymphatic drainage.[20] Miles[20] had described the lateral ligaments as existing between the pelvic fascia and levator muscles and, therefore, the operative emphasis was placed on wide resection of the levators. Waugh and Kirklin[40] and Sauer and Bacon,[39] however, argued that lateral lymphatic spread had been inadequately considered in these earlier studies and that this resulted in inadequate surgical resection. The theoretic justification for the RAPL was based on this improved understanding of lymphatic drainage patterns of carcinoma.[41]

EXTENT OF LYMPHATIC EXCISION FOR RECTAL CANCER

Wide Mesenteric Resection and High Ligation of the IMA

The IMA is the major pathway along which lymphatics from the rectosigmoid and left colon course en route to the para-aortic lymph nodes. The spread of colorectal cancer to lymph nodes along the IMA and its proximal branches has been examined extensively. In 1952, Grinnell and Hiatt[42] discovered metastases from rectal and sigmoid carcinoma to IMA lymph nodes proximal to its bifurcation in 7 of 41 (17 percent) patients undergoing abdominoperineal resection (APR) or low anterior resection with IMA ligation at the aorta. The authors[42] suggested that high ligation of the IMA "permits higher and more complete lymph node removal and should therefore raise the survival rate appreciably." Similar results for high ligation of the IMA were reported in 1954 by McElwain *et al.*[43] The authors examined 90 cases of resected rectosigmoid carcinoma with ligation of the IMA at the aorta. In 16 cases (17.8 percent), metastatic lymph nodes were found at the origin of the IMA. In eight (9 percent) of these cases, ligation of the IMA below the left colic artery would have left behind involved lymph nodes. The authors stated that these cases would have been "operative failures" without high ligation. Morgan and Griffiths[44] reviewed 214 cases of rectosigmoid cancer and noted a 16 percent incidence of C2 disease (presence of metastatic cancer immediately below ligature) prior to high IMA ligation. The incidence of C2 disease decreased to 8 percent when routine high IMA ligation was employed. Routine high IMA

ligation could thus convert 1 in 8 C2 cases into stage C1 (uninvolved lymph node immediately below ligature). Despite these findings it remained unknown whether high ligation of the IMA would impact upon survival. Enthusiasm for the concept, however, was evidenced by the appearance of detailed descriptions of the technique.[45, 46]

In 1962, Rosi *et al.*[45] retrospectively examined the result of the extent of mesenteric resection and level of ligation of the IMA on five-year survival from 1945 to 1955. Prior to 1950, carcinomas of the left, rectosigmoid, and rectum were treated by segmental resection (with APR for rectal cancer). After 1950, left hemicolectomy with ligation of the IMA at the aorta was performed instead of segmental resection. Patients who underwent high ligation of the IMA and more extensive mesenteric resection had an improvement in 5-year survival of 13.8 percent, 5.1 percent, and 6.9 percent for carcinomas of the left rectosigmoid, and rectum, respectively. A similar retrospective study was carried out by Grinnell[47]; patients with left colon and rectal cancer underwent resection with high IMA ligation. Of these, 19 (10.6 percent) had lymph node metastases between the aortic ligature and the first IMA branch. Seventeen of these patients were followed: 16 died with recurrent disease, while 1 was alive with advanced disease. Additionally, five-year survival was compared between 151 patients who underwent resection and high IMA ligation to 150 patients with IMA ligation below its bifurcation. An overall 5.7 percent survival advantage was found for those patients undergoing high ligation of the IMA. This survival advantage increased to 7.3 percent when only patients with Dukes C cancers were considered. Neither of these improvements, however, was statistically significant. Similar results were recently reported by Pezim and Nicholls[48] in their evaluation of 1,370 patients who underwent resection of rectosigmoid cancer; 784 had ligation of the IMA below the left colic artery and 586 patients had the IMA ligated at the aorta. No survival advantage could be demonstrated for the high ligation group. In fact, the high ligation group fared significantly worse when only stage C2 was considered (highest node below ligation contains metastatic cancer).

The cumulative data suggest that wider mesenteric resections and high ligation of the IMA do not improve five-year survival after resection of left colon and rectal cancer (Table 1). Ferguson *et al.*[49] had earlier reported five-year survival rates for segmental resection which were similar to more radical operations for rectosigmoid cancers. Grinnell[47] suggested that when high IMA nodes are involved with metastatic cancer, the disease had already, at least microscopically, spread beyond the scope of surgical treatment. Para-aortocaval as well as paraportal lymphatic spread can occur *via* accessory lymphatic channels, and this may be another reason for the failure of high IMA ligation to alter survival. Other important routes of lymphatic spread are not addressed by simple high ligation of the IMA and include the lateral rectal (lymphatics residing along the middle hemorrhoidal vessels) and iliac lymphatics. Thus, more aggressive surgical approaches have been advocated to include these regions within the resection and improve survival.

Table 1.
Survival Following Distal Colon and Rectal Resection with High and Low IMA Ligation

Reference	Year	Randomized Y/N	Prospective Y/N	Retrospective Y/N	5-Year Survival Low IMA Ligation* (%)	5-Year Survival High IMA Ligation† (%)	Survival Advantage (%)	*P*
Rosi *et al.*[45]	1962	N	N	Y	66.4	73.2	6.8	—‡
Grinnell[47]	1965	N	N	Y	—‡	—‡	5.7	NS
					—‡§	—‡§	7.3	NS
Pezim *et al.*[48]	1984	N	N	Y	89.8‖	86.3‖	None	NS
					57.6§	48.6§	None	NS

* Below ascending branch of left colonic artery.
† At origin from aorta.
‡ Actual percentage not reported.
‖ Dukes B cancers only.
§ Dukes C cancers only.

RAPL for Rectal Cancer: Surgical Technique

The technical aspects of abdominopelvic lymphadenectomy have been well-described[50–52] and are summarized here briefly. A thorough knowledge of the pelvic retroperitoneal anatomy is important to understanding this operation and is illustrated in Figures 2 and 3. Mobilization of the descending and sigmoid colon and identification of the ureters is performed in standard fashion. The parietal peritoneum is incised just below the duodenum (the superior extent of the dissection), and a complete lymphadenectomy is performed along the adventitial surface of the aorta and vena cava in a caudal direction. The inferior mesenteric vein is ligated just inferior to the duodenum and the inferior mesenteric artery is ligated flush with the aorta. The left colon is divided. The parietal peritoneum is incised over the pelvic brim and the dissection is extended onto the common iliac arteries; it is along this plane that the lymphadenectomy is extended into the pelvis. The ureters serve as the lateral boundaries of the dissection in the abdomen and the pelvis. The rectum is then mobilized off the sacrum using sharp dissection along the parietal pelvic fascia, ensuring *en bloc* resection of the mesorectum. The lateral ligaments are placed under medial traction and divided. The low rectum is mobilized by incising Waldeyer's fascia under direct vision allowing full mobilization of the rectum down to the levator ani muscles posteriorly and laterally. Anteriorly, the peritoneum is incised 1 to 2 cm above the reflection. Dissection then proceeds within Denovillier's fascia or the rectovaginal septum. The posterior vaginal wall can be resected if necessary. The lateral dissection includes sharp dissection of all of the fatty connective tissue and lymphatics surrounding the external and internal iliac vessels, superior vesicle, superior gluteal and obturator arteries, and from the obturator foramen. The area of dissection encompassed by RAPL is depicted in Figure 4. The operation is

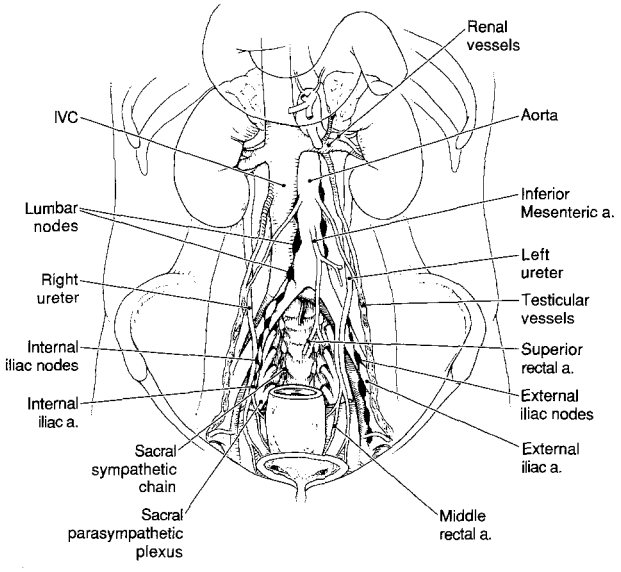

Figure 2. Anterior view of normal pelvic anatomy.

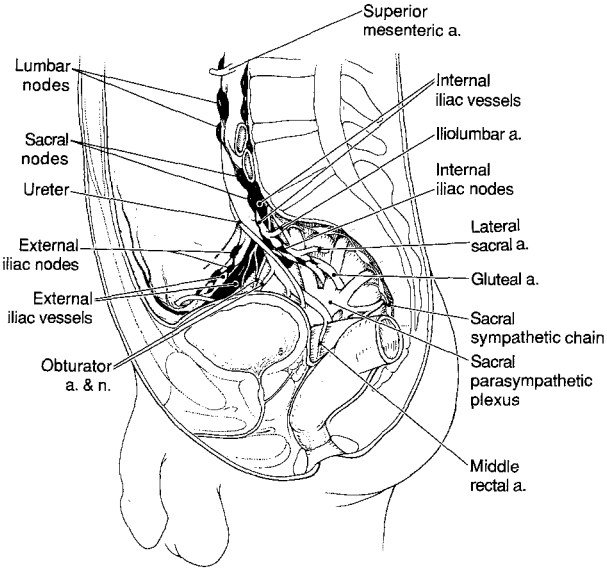

Figure 3. Lateral view of normal pelvic anatomy.

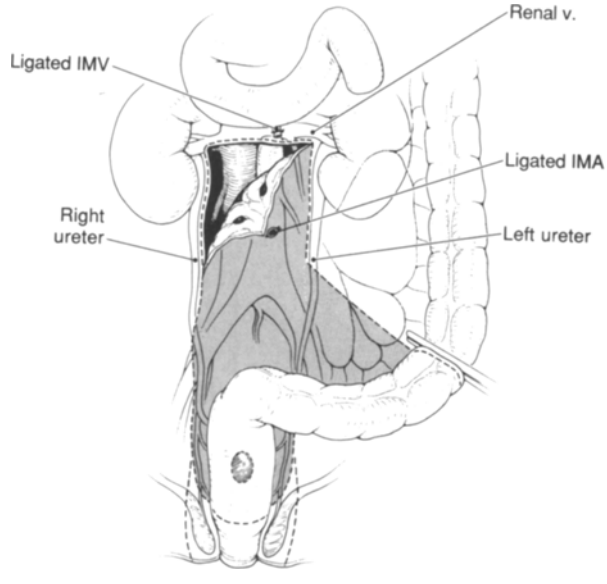

Figure 4. Operative boundaries of the radical abdominopelvic lymphadenectomy. RAPL can be performed in conjunction with low anterior resection or abdominoperineal resection depending on the location of the tumor.

completed by either perineal resection of the rectum or restorative resection, depending on the location of the tumor. This technique allows *en bloc* resection of all draining rectal lymphatics with the specimen.

Patient Selection

RAPL, employed with either anterior resection or APR, requires more extensive dissection and may be associated with an increase in morbidity compared with conventional resection. Thus, selecting patients likely to benefit from more aggressive resection would be of value. The aim of RAPL is to improve survival by *en bloc* clearance of regional lymphatics which may harbor occult metastases; it is important to identify such patients preoperatively. The likelihood of lymphatic metastases from rectal cancer is known to be associated with the pathologic stage of the primary tumor.[53, 54] Tumors confined to the submucosa are associated with a 0 to 5 percent chance of lymph node metastases. The risk of lymphatic metastases ranges from 10 to 27 percent with penetration into (but not through) the muscularis propria and increases to 70 percent with tumor penetration through the wall. Early cancers limited to the rectal wall have been successfully treated by local excision without compromising local control and with five-year survival rates of approximately 85 percent.[55–61] Such excellent results are attributable to the absence of lymph node metastases, and such patients should not be subjected to radical surgical resections such as RAPL.

Assessment of depth of rectal wall invasion has previously been accomplished by physical examination and CT scan. More recently, endorectal ultrasound staging has emerged as a more accurate diagnostic tool to assess both the extent of rectal wall penetration and the likelihood of perirectal lymph nodes metastasis.[62–66] Patients who have tumors limited to the rectal wall (uT1 or uT2) have a low likelihood of regional node metastases and thus should not be subjected to an extensive lymphadenectomy. However, rectal cancers that penetrate through the muscularis propria (uT3 and uT4) have a high risk of lymph node involvement. It is this group of patients (TNM Stage III rectal cancers) for whom RAPL would be of the most benefit.

EARLY TRIALS OF RAPL

Clinical evaluations of the extent of lymphatic resection for carcinoma of the rectum began in the late 1940s. The influence of lymph node involvement on survival for surgically resected rectal cancer below the peritoneal reflection was reviewed by Gilchrist and David.[67] These authors reported a five-year survival of 74.4 percent for patients without lymph node involvement and 37.5 percent with positive nodes. Similar results of 66 percent and 23.3 percent, respectively, were published by Waugh and Kirklin.[40] Even poorer survival rates for node-negative and node-positive low rectal cancers of 53.2 percent and 16.6 percent, respectively, were reported by Pfeiffer and Miller.[68] This data led to the reappraisal of then current operative techniques. Sauer and Bacon[39] proposed that the poor survival for surgically treated rectal cancers below the peritoneal reflection was attributable to inadequately resected lateral lymphatic spread. The evolution of these concepts is exemplified in the reports by Ault and Castro[50, 69, 70] Their initial efforts from 1940 to 1950 involved simple, high ligation of the inferior mesenteric vessels. Improved understanding of patterns of lymphatic metastases and its impact on survival led to progressively more radical surgical techniques.

Rectosigmoid tumors (above the peritoneal reflection) most often metastasize to the lymph nodes along the superior hemorrhoidal vessels and are easily resected. Satisfactory resection of the lateral lymphatics for low rectal cancers is technically more difficult. Sauer and Bacon[71] contended that the original description of this region by Miles[20] led to inadequate resection of low rectal cancers and a poorer outcome. They emphasized that the endopelvic fascia was an important lymphatic structure which required intact separation from the pelvic side walls. They also advocated complete dissection of the lymphatics off the iliac vessels. State,[72] in 1951, described and advocated routine application of RAPL for the management of rectal cancer, citing the well-studied anatomic pathways of proximal metastatic spread of rectal cancer as its scientific foundation.

A 50 percent pelvic recurrence rate after APR for rectal cancer at the Memorial Hospital motivated Deddish[73] to propose a more aggressive initial effort to remove the primary tumor and the regional lymphatics. He reported one of the first studies of

RAPL with APR for rectal cancer. In the first 25 cases of advanced cancer (annular or ulcerated cancers, or those with submucosa induration), lymph node metastases were present in 24 percent. These tumors would have been outside the area resected by the standard Miles operation. In a follow-up series [75] of 70 patients, the frequency of lymph node metastases was 16 percent. An increase in surgical morbidity (predominantly bladder dysfunction and hemorrhage) was noted, although operative mortality was not different from conventional operation.

Sauer and Bacon[71] reported their initial results with abdominoperineal resection and RAPL for upper and lower rectal cancers in 32 patients. The cephalad limit of their dissection was just above the IMA. In the 12 cases of cancer located above the middle valve of Houston (approximately 7 cm from the anal verge), lateral lymphatic spread was not present. However, 6 of 20 patients (30 percent) with low rectal cancers (*e.g.*, below the middle valve) had lateral lymphatic metastases. This study confirmed the results reported by Deddish,[73] although no survival data were presented.

Bacon *et al.*[74] reported survival data in 80 patients who underwent resection with RAPL for carcinoma of the rectum and distal left colon. Five-year survival was 60 percent for the entire group and 53.4 percent for patients with low rectal cancers. This represented a statistically insignificant improvement in survival from their data reported in 1949 (55 percent and 49.5 percent, $P > 0.05$). Five-year survival was only 27 percent when metastatic lymph nodes were found at the origin of the IMA. One would have expected an improvement in five-year survival in this subgroup with more extensive lymphadenectomy.

Shortly after the report by Bacon *et al.*,[74] Sterns and Deddish[75] published their experience with 122 patients who underwent RAPL with either abdominoperineal or low anterior resection for cancers located below 20 cm from the anal verge. Metastases to abdominopelvic lymph nodes outside the area encompassed by conventional resection were found in 9 percent of all patients and in 17 percent of those with Dukes C lesions. The overall five-year survival rate was 54 percent for this group compared with only 46 percent for 442 patients who underwent standard resection. This difference was not statistically significant. Survival improvement for patients with Dukes C disease undergoing RAPL was more dramatic. These patients had a five-year survival rate of 40 percent compared with only 23 percent for historic controls who had undergone standard resection. This difference approached statistical significance but was diminished by the small sample size. Of 37 evaluable patients who died of metastatic cancer, 23 (60 percent) had residual disease in the pelvis despite the more extensive lymphatic resection. Complication rates, blood loss, and hospitalization time were significantly increased in the group who underwent RAPL. Sterns and Deddish[75] concluded that there was no justification for more radical abdominopelvic lymphatic resection.

Little or no benefit for aggressive lymphadenectomy was reported in the literature over subsequent years. Ferguson *et al.*[49] reported five-year survival rates for segmental resections of rectal, rectosigmoid, and sigmoid cancers which were comparable to more radical operations. Grinnell[76] reviewed 22 cases of rectal cancer in which atypical lymphatic spread was found. This included intramural spread more than 1 cm distal to the tumor, extramural involvement of pararectal nodes at least 1.5 cm distal to the tumor, or metastatic involvement of middle hemorrhoidal or deep pelvic lymph nodes. Distal extramural and retrograde nodal involvement were noted to usually occur when the proximal lymphatics were blocked. Patients with this pattern of distal nodal metastases did not survive five years, reflecting an extent of disease unaffected by the extent of surgical resection. Thus, Grinnell[76] discouraged the use of radical lymphatic excision. Harvey and Auchincloss[77] reviewed survival data from 1,560 patients who underwent colorectal resections from 1938 to 1954. In patients with metastases in five or more lymph nodes, only those with nodes within 5 cm of the tumor were likely to be long-term survivors. Also, when fewer than five positive nodes were present, they were usually adjacent to the tumor. There were no survivors when metastatic lymph nodes were present at the base of the mesentery. It was concluded that surgery was unlikely to cure any patient when metastatic lymph nodes were not confined to the immediate proximity of the primary tumor. A similar failure to improve outcome with lymph node dissection was reported by Dwight *et al.*;[78] however, details of this study were not presented. All of

these data, which discouraged aggressive resection and lymphadenectomy for colorectal cancers, were retrospective and nonrandomized. Recent efforts have continued to clarify the potential role of RAPL in the management of rectal cancer.

RECENT EXPERIENCE WITH RAPL FOR RECTAL CANCER

Over the past decade, experience with RAPL as an adjunct to conventional resection for rectal cancer has accumulated from only a few centers. The largest experience has been reported from the National Cancer Center in Japan.[24-26] Other large series have been published from St. Mark's Hospital in London,[51] the University of Chicago,[22, 79] and Memorial Sloan-Kettering Cancer Center.[23] These institutions with expertise in performing RAPL have reported morbidity and mortality rates which are slightly increased over more conventional resections (Tables 2 and 3). All of these most recent data are also from nonrandomized, retrospective studies and require careful interpretation. The cumulative worldwide experience with RAPL, including reported five-year survival and local recurrence rates compared with conventional resection, is depicted in Table 4.

Enker *et al.*[22] in 1979 reported the initial University of Chicago experience with wide resection for carcinoma of the colon and rectum in 216 patients operated on between 1966 and 1970. The five-year survival was 45.5 percent for the 48 patients with rectal cancer. Among the 14 patients with GITSG C2 tumors, 11 underwent iliac lymph node dissection. Two patients (18.2 percent) developed local recurrences. The three patients who did not have extended node dissection all developed local recurrences. A survival advantage was reported for 65 patients with Astler-Coller C1 and C2 lesions when more than 10 nodes were found in the resected specimen (mean survival = 53.2 months with 1 to 10 nodes *vs.* 71.2 months with >10 nodes), suggesting a therapeutic benefit associated with wide pelvic and mesenteric resection. This group, however, included colonic as well as rectal cancers. Definitive conclusions from these small subsets of patients could not be made.

Enker *et al.*[23] subsequently reported results from a series of 412 patients, 220 of whom underwent conventional resection for rectal cancer, while 192 had *en bloc* pelvic lymphadenectomy (RAPL) and with proctectomy. No statistically significant survival difference between the two groups was found for Stage A or B rectal cancers, whether defined by Dukes classification, or the Astler-Coller or GITSG modification of Dukes stage. However, a survival advantage was noted for patients who underwent RAPL compared with conventional resection for Astler-Coller stage C1 (81 percent *vs.* 41 percent, $P \leq 0.03$), GITSG stage C1 (54 percent *vs.* 33 percent, $P \leq 0.03$), and Dukes C tumors (48 percent *vs.* 29 percent, $P \leq 0.03$). A trend toward survival improvement was noted in the RAPL group of patients with Astler-Coller and GITSG C2 tumors.

Table 2.
Morbidity and Mortality of RAPL Compared with Conventional Resection CONV

Reference	Year	No. of Patients with CONV	No. of Patients with RAPL	Morbidity			Mortality (%)		
				CONV	RAPL	*P*	CONV	RAPL	*P*
Bacon *et al.*[74]	1958	—*	80	—	—	—	—	3.1	—
Stearns and Deddish[75]	1959†	442	122	—	—	—	—	2.5	—
Enker *et al.*[22]	1979	—	216	—	9.7	—	—	6.4	—
Koyama *et al.*[24]	1984†	218	163	—	—	—	—	1.4	—
Glass *et al.*[51]	1985†	2266	75	86	69	NS	—	2.7	—
Enker *et al.*[23]	1986†	220	192	—	—	—	2.3	1.6	NS
Moriya *et al.*[26]	1989†	102	232	—	—	—	2.9	0.4	NS
Hojo *et al.*[25]	1989†	245	192	16.9‡	22.8‡	NS	1.2	2.1	NS
				8.2§	6.8§	NS			
				4.1‖	4.2‖	NS			
Michelassi *et al.*[81]	1992†	10	17	40¶	47.1‖	NS	0.0	0.0	NS

* — = not reported.
† Rectal cancers only.
‡ Anastomotic leak.
§ Pelvic infection.
‖ Bowel obstruction requiring surgery.
¶ Early postoperative.

Table 3.
Series Reporting Morbidity of RAPL Compared with Conventional Resection (CONV)

Reference	Year	Intraoperative Blood Loss		Hospitalization		Impotence		Urinary Dysfunction	
		CONV	RAPL	CONV	RAPL	CONV (%)	RAPL (%)	CONV (%)	RAPL (%)
Stearns and Deddish[75]	1959	1–2 units	4–5 units	7–10 days (longer with RAPL		—*	—	—	19†
Koyama *et al.*[24]	1984	X	X + 150 ml	—	—	—	100	—	100‡
Glass *et al.*[51]	1985	—	—	—	—	—	—	34	26
Enker *et al.*[23]	1986	Transfusions > 2000 ml		—	—	—	—	10	26
		10%	12%						
Hojo *et al.*[25]	1989	1500 ml	1900 ml	—	—	37.5§	76§	8.8‖	39.4‖
								48¶	80¶
								3.4#	3.0#
Michelassi *et al.*[81]	1992	1612 ml	1616 ml	12.1	11.7	33	—	10	18
				Intraoperative blood loss > 2000 ml					
		10%	18%						
Enker[52]	1992	—	630 ml	—	—	13	—	—	—

* — = not reported.
† Major urologic complications.
‡ Ninety-one percent able to void six months after operation.
§ Impotent; under 60 years of age.
‖ Loss of sense of bladder fullness at one year.
¶ Postoperative "bladder complications."
# Requiring self-catheterization at one year.

Table 4.
RAPL for Colorectal Cancer *vs.* Conventional Resection (CONV): 5-Year Survival/Local Recurrence

References	Year	No. of Patients with CONV	No. of Patients with RAPL	Prospective/ Randomized Y/N	Retrospective Y/N	5-Year Survival (%)			Local Recurrence (%)		
						CONV	RAPL	*P*	CONV	RAPL	*P*
Bacon *et al.*[74]	1958	*	80	N	Y	55	60	NS	*	*	*
Stearns and Deddish[75]	1959	442	122	N	Y	46†	54†	NS	*	*	*
						23‡	40‡	NS	*	*	*
Enker *et al.*[22]	1979	—§	216	N	Y	—	65.5	*	—	—	*
			34‖			—	63.3‖	*	—	16‡¶	*
Koyama *et al.*[24]	1984#	218	163	N	Y	63.7¶	83.2¶	0.01	26.1¶	8.4¶	0.01
						30.8‡	52.5‡	0.02	44.3‡	24.5‡	0.01
Glass *et al.*[51]	1985#	2266	75	N	Y	56.6	54.5	NS	—	13.6	*
Enker *et al.*[23]	1986	220	192	N	Y	54.3†	63.8†	0.026	*	*	*
						83.9[a]	84.9[a]	NS	13.6[a]	13.4[a]	NS
						61.5¶	52.5¶	NS	23.4¶	38.3¶	NS
						28.8‡	48.3‡	0.03	46‡	35.5‡	NS
Michelassi *et al.*[79]	1988#	73	64	N	Y	Not assessed			16.4	9.4	0.16
Moriya *et al.*[26]	1989#	102	102	N	Y	67.4†	75.8†	NS	17	12	NS
						83¶	86.7¶	NS			
						43.7‡	68‡	NS			
Hojo *et al.*[25]	1989	245	192	N	Y	91.1[a]	94.3[a]	NS	5.2	0	NS
						74.2¶	88.1¶	0.05	21.9	6.3	0.05
						43.2‡	61.3‡	0.05	32.8	23.6	0.05

* Number not reported.
† All Dukes stages.
‡ Dukes C rectal cancer.
§ — = group not represented in study.
‖ Subgroup with rectal cancer (Dukes D excluded).
¶ Dukes B rectal cancer.
# Rectal cancers only.
[a] Dukes A rectal cancer.

The incidence of pelvic recurrence was not significantly reduced by extended resection. In the subgroup of patients who underwent low, anterior resection for midrectal cancer only, more pelvic recurrences occurred in patients who underwent conventional compared with extended resection (54 percent *vs.* 32 percent, Dukes B; 60 percent *vs.* 31 percent, Dukes C without preoperative radiation therapy). This study was not randomized and the methods of patient selection for conventional *vs.* extended resection were not specified.

Experience with RAPL at St. Mark's Hospital from 1960 to 1981 was retrospectively reviewed in 1985.[51] Seventy-five patients underwent extended resection based upon local extension or unfavorable histologic grade. Patients were equally distributed between APR and low anterior resection. Fifty-five patients available for five-year follow-up who underwent resection with RAPL were compared with 2,266 patients who underwent conventional resection from 1948 to 1972. No improvement in crude five-year survival was observed for patients after extended resection (54.5 percent *vs.* 56.6 percent). Survival was worse for patients with Dukes C1 tumors (no metastatic disease at the origin of the inferior mesenteric artery) following extended resection (29.2 percent) than for the historic controls (40.4 percent). No improvement in local recurrence could be demonstrated.

Michelassi *et al.*[79] performed RAPL in 64 patients and compared the results with 73 patients who underwent conventional resection for rectal cancer. Recurrence rates were 9.4 percent and 16.4 percent, respectively, and were not statistically significantly different. Survival data were not reported. In this series, lymphadenectomy was begun at the aortocaval bifurcation instead of below the third portion of the duodenum.

The largest experience with RAPL for rectal cancer is from the National Cancer Center Hospital in Japan. The operation had been practiced in Japan for some 10 to 15 years prior to the first Japanese reports in the English literature in the early 1980s. Of the 423 patients who underwent RAPL from 1969 to 1980, 51.4 percent were found to have lymph node metastases, 23 percent of patients with low rectal cancers had lateral lymphatic spread, and 6 percent demonstrated inguinal node involvement. Poor survival was noted when lateral nodal metastases were present (16 of 17 patients died of recurrent disease within five years) and an aggressive surgical approach was advocated.[37]

Koyama *et al.*[24] reported their early experience with RAPL in 163 patients. The "extended" procedure involved resection of the internal iliac artery and vein if adjacent lymphatic tissue appeared to be involved by metastatic disease. This extended RAPL was performed on 74 patients with Dukes B cancer and 89 with Dukes C lesions. Five-year survival was 83.2 percent and 52.5 percent, respectively. The five-year survival for stage-matched historic controls who underwent conventional resection was 63.7 percent and 30.8 percent, respectively. This survival difference was statistically significant ($P < 0.05$). The incidence of local recurrence was also less in patients who underwent extended lymphadenectomy. Local recurrence for Dukes B lesions decreased from 26.1 percent to 8.4 percent and for Dukes C tumors there was a decrease in local recurrence from 44.3 percent to 24.5 percent ($P < 0.01$).

Hojo *et al.*[25] subsequently reported the results of 192 patients who underwent RAPL and 245 who had conventional lymphadenectomy with either APR or low anterior resection for middle and lower third rectal cancer. Cumulative five-year survival rates for patients who underwent extended resection were 88 percent for Dukes B cancers and 61 percent for Dukes C cancers. Those who underwent conventional resection had a five-year survival of 74 percent for Dukes B and 43 percent for Dukes C tumors. Local recurrence rates were significantly less after extended resection compared to conventional resection for Dukes B (6.3 percent *vs.* 21.8 percent) and Dukes C (23.6 percent *vs.* 32.9 percent) cancers. All comparisons were statistically significant ($P < 0.05$). In another analysis of these data,[26] a five-year survival rate of 49 percent was reported for patients with lateral node metastases who underwent extended resection; this was markedly better than the near zero survival previously reported after conventional resection.[37]

COMPLICATIONS OF RAPL

Efforts to improve survival by utilizing more radical lymphatic excision have been accompanied by increased morbidity, particularly urinary and sexual dysfunction (Tables 2 and 3). Hojo *et al.*[25] reported an 80 percent incidence of bladder dys-

function after RAPL compared with 48 percent for conventional resection. Inability to sense bladder fullness was reported in 39.4 percent and 8.8 percent of these patients, respectively. An inability to void persisted after one year in 3 percent of patients after RAPL. Impotence occurred in 76 percent of male patients after RAPL compared with 37.5 percent who underwent conventional resection. Refinements in operative technique and attention to the details of pelvic dissection have decreased the incidence of urinary dysfunction. Hojo *et al.*[80] subsequently reported maintenance of bladder function with preservation of only the fourth pelvic parasympathetic nerve root unilaterally. The incidence of sexual dysfunction in this study, however, remained 70 to 80 percent. Other recent studies have also demonstrated a decrease in morbidity when autonomic nerve preservation is practiced during RAPL. In a series by Enker,[52] 86.7 percent of patients remained potent and 87.9 percent had normal ejaculatory function. Michelassi and Block[81] have also reported low rates of bladder dysfunction. Intermittent self-catheterization for neurogenic bladder was required in only 18 percent of patients after RAPL and all recovered bladder function eight months after operation.

Operative mortality rates for RAPL are acceptably low and range from 0.4 to 6 percent[22-26, 51, 81] (Table 2). Intraoperative blood loss has been reported to be significantly higher after extended lymphadenectomy by Moriya *et al.*[26] However, Michelassi and Block[80] have not reported higher mean intraoperative blood loss with RAPL. Additionally, the length of postoperative hospitalization after RAPL is no longer than after conventional resection.[81]

CONCLUSIONS AND STRATEGY FOR THE FUTURE

In 1993 there will be approximately 7,000 deaths in the United States from rectal cancer.[1] Existing treatment modalities have marginal survival benefit for patients with metastatic disease. Five-year survival rates for patients undergoing curative resection for adenocarcinoma of the rectum range from 45 to 65 percent.[6, 8-10, 15-19, 82-85] Locoregional recurrence rates range from 5 to 45 percent depending upon tumor stage and series examined.[5,6,13,15,84-92] Pelvic recurrence is directly related to tumor stage and is associated with extremely poor patient life-style and survival.[84, 86] Initial efforts which reduce the incidence of pelvic recurrence may, however, improve survival. A reduction in local recurrence rates from rectal cancer has been achieved in several studies by employing chemotherapy and radiation therapy.[14-19, 93] Adjuvant chemoradiation is more effective than either chemotherapy or radiation therapy alone.[15, 19] Unfortunately, improvement in overall survival has not been consistently demonstrated in these prospectively randomized trials.[15-17, 19] In an effort to improve existing survival statistics for locally advanced rectal cancer, several centers have utilized RAPL.[22-26, 50, 51, 79] These results have been variable (Table 4). Furthermore, investigations have not been prospective or randomized and all have involved historic controls. Nevertheless, data have now accumulated from respected oncologic surgical centers which suggest that patient outcome can be improved by surgical technique. RAPL for selected cases of rectal cancer may decrease local recurrence and improve survival.[22-26, 51, 79]

The impact of surgical technique on patient outcome has also been reported by Heald and coworkers.[13, 90-92] Heald's group has routinely performed routine total mesorectal excision (TME) for rectal cancer and reports local recurrence rates of 3.5 to 5 percent after curative resection.[90-92] MacFarlane *et al.*[92] reported their recent experience with TME for advanced rectal cancer (Dukes B2 and C). Data were compared with a stage-matched group of patients who underwent adjuvant radiation (RT) or chemoradiation therapy in the study reported by the North Central Cancer Treatment Group.[19] The survival and recurrence data for TME was better, stage for stage, than the those of the adjuvant-treated group in the North Central Cancer Treatment Group trial. Five-year local and overall recurrence for TME was 5 percent and 22 percent, respectively. In the North Central Cancer Treatment Group trial,[19] chemoradiation resulted in five-year local and overall recurrence rates of 13.5 percent and 41.5 percent. This increased to 25 percent and 62.7 percent, respectively, when RT was used alone. Heald's group[92] also reported a five-year tumor-free survival of 78 percent in these high-risk patients. These data support the concept that surgical technique may be a more important therapeutic variable than adjuvant therapy.

A prospective, randomized, controlled study comparing conventional resection with RAPL has

not been done. Even comparison of high *vs.* low ligation of the inferior mesenteric artery has not been evaluated in a randomized, prospective fashion. Adjuvant treatment of rectal cancer with chemotherapy and radiation therapy appears to improve local control of disease.[14–19, 93] Although encouraging, these results may lead surgeons to a nihilistic attitude toward the technical aspects of managing rectal cancer. This may be particularly true in view of the recent trend toward minimally invasive colon and rectal surgery. In contrasting the difficulty of conducting randomized, controlled trials of surgical therapy for rectal cancer to related noninvasive medical therapies, Fielding[94] recently pointed out that, "Critical identification of the best surgical therapy, especially for complex procedures, is much more difficult. Difficult or not, it is high time for the surgical scientific community to tackle this issue more effectively." Nonrandomized studies of adjuvant chemoradiation therapy for rectal cancer have culminated in prospective, randomized trials. These trials have clearly demonstrated benefit for patients with advanced disease. Benefit of extended surgical resections (RAPL) for rectal cancer have similarly been demonstrated in multiple nonrandomized studies. This information should serve as the foundation upon which to base a prospective and properly randomized trial.

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