

Survival After High or Low Ligation of the Inferior Mesenteric Artery During Curative Surgery for Rectal Cancer

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In an attempt to determine whether "high ligation" of the inferior mesenteric artery during surgery for cancer of the rectum and rectosigmoid confers any significant 5-year survival advantage over "low ligation," the outcome of 1370 patients was reviewed. There were 784 patients in whom the inferior mesenteric artery was ligated below the origin of the left colic artery (low ligation) and 586 in whom it was ligated above this level (high ligation). The distribution of histologic grades of the tumors and incidence of venous invasion were similar in both groups. Five-year follow-up was complete in 98.5%. No difference in the crude or age-corrected 5-year survival was found for patients with Dukes A, B, C overall, or C₁ tumors, whether having had a low or high ligation. In hopes of identifying a population that benefited from high ligation, C₁ patients were further subgrouped according to tumor location and number of involved lymph nodes. However, in no such subgroup was any significant high ligation advantage seen. In conclusion, high ligation of the inferior mesenteric artery has not been found to improve 5-year survival in patients with cancer of the rectum or rectosigmoid.

IN 1908 W. ERNEST MILES POSTULATED that the almost total failure to cure cancers of the rectum and sigmoid colon was the result of inadequate removal of "the zone of upward spread." Until that time, he and most of his contemporaries had relied solely upon perineal methods of excision of these tumors. After observing that patients dying of rectal cancers exhibited proximal intra-abdominal lymph node involvement, Miles attempted to improve the dismal prognosis by developing the abdominoperineal procedure, incorporating the transabdominal removal of lymphatic tissues. Believing that the route of lymphatic drainage of the rectum lay along its arterial supply, he recommended division of the inferior mesenteric artery (IMA) just distal to the left colic branch, with a subsequent *en bloc* excision of nodes and bowel below.¹

While Miles' plea for the removal of a certain amount of proximal lymphatic tissue is generally accepted by most surgeons today, the optimum level of lymphovas-

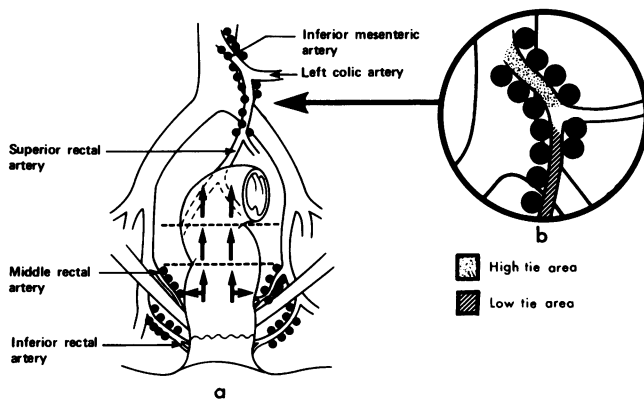
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cular division has remained controversial ever since the concept was introduced. Within the same year as the description of the abdominoperineal operation, Moynihan argued that ligation and division of the inferior mesenteric artery should be flush with the aorta in order to remove even more proximal lymph nodes. He noted, "We have not yet sufficiently realized that the surgery of malignant disease is not the surgery of organs; it is the anatomy of the lymphatic system."² When Dukes subsequently showed that upward lymphatic extension of cancer is confined with remarkable consistency to the glands intimately related to the inferior mesenteric artery right to the aorta, Moynihan's "high tie" became a logical extension of radical excision of rectal cancer.³ Subsequent reports of patients whose high tie operative specimens showed involved nodes above the level of the left colic artery seemed to prove the inadequacy of the "low tie" advice of Miles.^{4,5} In particular, the finding of Gabriel, Dukes, and Bussey⁶ that survival was better if the node adjacent to the inferior mesenteric artery ligature was not involved with tumor (Dukes C₁), than when it was (Dukes C₂), added support for the high tie. This led Morgan to postulate that the maneuver could sometimes convert what would have been a C₂ case, if treated by a low tie, into a C₁ case with a correspondingly better prognosis if treated by a high tie.⁷

Thus it was a great disappointment when reports of poor survival after high ligation began to appear in the literature.^{8,9} Those individuals with involved nodes above the left colic artery, precisely the ones for whom the high tie was supposed to have been most advantageous, did not appear to have any better prognosis than others treated more conservatively. One explanation given for this apparent failure of high ligation is the presence of lateral lymphatic drainage routes of tumors of the lower third of the rectum.¹⁰ Such alternate pathways of spread would frustrate any attempts at tumor control by inferior

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Submitted publication: November 1, 1983.



FIGS. 1a and b. *a.* Direction of lymphatic drainage of lower, middle, and upper rectum. *b.* Location of high and low tie areas along the inferior mesenteric artery. Reproduced by kind permission of J. B. Lippincott Co. "Essentials of Ano-Rectal Surgery," Goldberg, Gordon, and Nivatvongs.

mesenteric artery ligation, regardless of the level of the tie. Another factor could be the generally poor prognosis of rectal cancer patients with more than five involved lymph nodes who, if included in studies of high ligation, might obscure its value. Yet there have been no reports of the value of high ligation in patients whose tumors are located in the upper two-thirds of the rectum or who have fewer than five involved lymph nodes.

Accordingly, we have reviewed the outcome of 1370 patients who have undergone surgical treatment for cancer of the rectum and rectosigmoid at St. Mark's Hospital. Survival after low and high ligation has been compared, with particular emphasis on individuals whose tumors were in the upper two-thirds of the rectum and in whom less than five lymph nodes were involved.

Method

The records of all patients receiving surgical treatment for cancer of the rectum or rectosigmoid during the period 1953 to 1972 were reviewed. Only those having potentially curative procedures producing stageable specimens were considered for study. Cases with an uncertain location of lymphovascular division, immediate adjuvant therapy, or macroscopic tumor encroachment upon the anus were discarded. Wide pelvic lymphadenectomy is rarely practised at St. Mark's, and no such cases have been included in this study.

Patients were divided into two groups; "low tie" in whom division of the inferior mesenteric artery was below the left colic artery, and "high tie" in whom it was above (often flush with the aorta, Fig. 1). During the period of study, nine surgeons were on the staff of the hospital. Of these, three preferred the high tie maneuver as a routine, while six preferred the low tie.

The decision as to whether the disease was disseminated or not depended largely upon the findings at

laparotomy since most of the patients were treated in the pre-computerized tomography (CT) and ultrasound era. All, however, had a preoperative chest x-ray. The survival rates of rectal cancer previously reported from St. Mark's have been based on this method of defining dissemination. Any errors in the definition of metastases would apply to both low and high tie groups.

On examination by the pathologist of the excised specimen, tumors were staged according to the Dukes' classification, including the subdivision of Dukes' C into Dukes' Stages C₁ and C₂. In both C₁ and C₂ stages nodes are present; in C₂ the highest node below the ligation contains metastatic disease, while in Stage C₁ it does not. The level of cancer in the rectum was determined by sigmoidoscopy before surgery and by postoperative examination of the specimen. Tumors were sited as follows: lower rectum (4–8 cm from the anal verge), middle (8–12 cm), upper (12–16 cm), and rectosigmoid.

Long-term survival was expressed as crude 5-year survival and age-corrected 5-year survival rates. Age correction factors were based upon life-tables for England and Wales for the appropriate years. Statistical analysis was carried out by the chi squared method.

Patients

One thousand, three hundred seventy patients fulfilled the criteria for inclusion, of whom 784 (57.2%) had a low tie and 586 (42.8%) a high tie. Five-year follow-up was complete in 98.5%, the 17 patients who were lost to follow-up were equally divided between the low and high tie groups (nine and eight, respectively). Those patients were presumed to have died of cancer. Mean age was greater in the low tie group (65.1 years vs. 58.6 years).

The distribution of Dukes' Stages is shown in Table 1. There were more Dukes' A Stage patients in the low tie group ($p < 0.05$) and more C₁ patients in the high tie group ($p < 0.05$). There was no difference in the distribution of B and C₂ cases between the low and high tie groups. There were no statistically significant differences between the groups with respect to the location of the tumor in the rectum, histologic grade, presence of venous invasion, or the extent of local spread (Tables 2–4).

Nine hundred seven of the patients were treated by abdominoperineal resection, 455 by anterior resection, six by the Hartmann operation, and two (with colitis) by proctocolectomy (Table 5).

Results

Operative Mortality

Thirty-seven patients died within 60 days of their surgery and were therefore classified as operative deaths.

There were 24 patients (3.1%) in the low tie group and 13 (2.2%) in the high tie group. This difference was not significant.

Complications

The rate of complications was almost identical, being 63.5% in the low tie group and 64% in the high tie patients. In particular, there were no significant differences in the incidence of sepsis or of anastomotic leakage, ischemic colitis, or gangrene of the colostomy.

Site of Treatment Failure

Unfortunately, in such a large series of patients, accurate information on the site of treatment failure is often not available. To do this satisfactorily, *post mortem* data would have to have been available in all, which they are not. However, the follow-up as far as date of death is concerned is accurately known in 98.5%, that is, in all but 17 of 1370 patients whose records were studied. Under the circumstances, one can only present survival rates based on large numbers.

Five-Year Survival (Table 6)

Age-corrected survival. There were no statistically significant differences in age-corrected survival between low and high groups overall. Neither was there any difference in those subgroups of patients with Dukes' A, B, C overall, or C₁ cancers. There was also no statistically

TABLE 1. *Distribution of Pathologic Stages*

	Dukes A	Dukes B	Dukes C ₁	Dukes C ₂	Total
Low Tie	164 (21%)	312 (40%)	261 (33%)	47 (6%)	784
High Tie	93 (16%)	234 (40%)	227 (39%)	32 (5%)	586
Totals	257	546	488	79	1370

significant difference in age-corrected 5-year survival after low or high ligation in either of the two C₁ subgroups, namely those with fewer than five nodes involved with or without exclusion of tumors of the lower one-third of the rectum. In Dukes' Stage C₂, patients in the high tie group fared significantly less well than similarly staged patients in the low tie group.

Crude survival. Prior to age correction, a significantly better survival ($p < 0.005$) was seen in the high tie Dukes A subgroup, and no significant crude survival difference was found in Dukes C₂ low and high tie groups, likely a reflection of the younger ages of the high tie patients.

Discussion

The results of the current series suggest that high ligation of the inferior mesenteric artery does not improve the survival of patients with rectal and rectosigmoid cancer. While comparing the outcome of all low tie patients to all high tie patients is probably unfair because of the greater number of Dukes' C₁ cases in the latter group, analysis of survival within each Dukes Stage

TABLE 2. *Tumor Location*

	Dukes A		Dukes B		Dukes C ₁		Dukes C ₂		Total	
	L	H	L	H	L	H	L	H	L	H
Rectosigmoid	19	13	36	25	14	22	6	5	75	65
Upper one-third of rectum	41	35	111	83	78	77	9	5	239	200
Middle one-third of rectum	48	26	83	76	92	77	16	10	239	189
Lower one-third of rectum	56	19	82	50	77	51	16	12	231	132
Totals	164	93	312	234	261	227	47	32	784	586

L—low tie; H—high tie.

TABLE 3. *Distribution of Histologic Tumor Grade and Pathologic Stage*

	Dukes A		Dukes B		Dukes C ₁		Dukes C ₂		Total	
	L	H	L	H	L	H	L	H	L	H
Low grade	77	43	97	71	32	17	1	1	207	132
Average grade	73	43	185	143	154	127	25	17	437	330
High grade	3	1	11	7	42	44	12	10	68	62
Colloid	11	5	19	13	33	39	9	4	72	61
Not graded	—	1	—	—	—	—	—	—	—	1
Total	164	93	312	234	261	227	47	32	784	586

L—low tie; H—high tie.

TABLE 4. Percentage of Patients with Venous Invasion

	Dukes A	Dukes B	Dukes C ₁	Dukes C ₂	Total
Low tie	0	81/312 (26%)	69/261 (26.4%)	10/217 (21.3%)	160/784 (20.4%)
High tie	0	52/234 (22.2%)	75/227 (33%)	9/32 (28.1%)	136/586 (23.2%)
Totals	0	133/546 (24.3%)	144/488 (29.5%)	19/79 (24%)	296/1370 (21.6%)

nevertheless does not show any advantage for high tie. Differences in survival of crude and corrected data in the low and high tie group can be accounted for by the relatively older age of the latter.

A similar conclusion was reached by Grinnell. In a 1952 publication⁴ he had reported 19 colon and rectal cancer patients whose excised high ligation specimens were found to contain involved nodes above the left colic artery. These nodes would have been left behind had a low ligation been performed, thus suggesting the value of the high tie. Subsequent follow-up, however, revealed that none of the 19 had been salvaged by the procedure, although one was lost to follow-up and one killed in an accident. He concluded that once tumor

had involved these high lymph nodes, it had probably spread beyond.⁸

Another important prognostic factor, that of the total number of involved lymph nodes, was described by Harvey and Auchincloss, who found that in 442 colon and rectal cancer patients surviving for at least 5 years only 3.2% had five involved nodes and only 2.8% had more than five.¹¹ In the few instances where more than five nodes were involved, they were all clustered close to the tumor. Accordingly, it has been postulated that a high tie in patients with a limited number of involved nodes might improve survival by advancing the margin of clearance. However, in our subgroup of C₁ patients with less than five involved lymph nodes, we were unable to provide any evidence for the value of the high tie in this situation (Table 6).

Although lymphatic drainage of rectal and rectosigmoid cancers is still thought to be primarily along the inferior mesenteric artery, other lymphatic routes do exist and may confuse the assessment of the high ligation (Fig. 1a). Tumors of the upper one-third of the rectum and rectosigmoid may drain along lymphatic channels that follow the portal vein and may be responsible for isolated lymphatic metastases in the porta hepatis.¹² In the lower one-third of the rectum drainage may occur

TABLE 5. Distribution of Pathologic Stage in Patients Treated by Anterior Resection and Total Rectal Excision

	Dukes A		Dukes B		Dukes C ₁		Dukes C ₂		Total	
	L	H	L	H	L	H	L	H	L	H
Anterior resection	64	56	101	101	44	70	11	8	220	235
Total rectal excision	99	36	210	131	214	157	36	24	559	348
Other	1	1	1	2	3	0			5	3
Totals	164	93	312	234	261	227	47	32	784	586

L—low tie; H—high tie.

TABLE 6. Five-Year Survival Rates After Low and High Ligation of the Inferior Mesenteric Artery Excluding Operative Deaths

Stage		Crude 5-Year Survival	Age-Corrected 5-Year Survival	Significance After Age Collection
Dukes A	Low	128/159 (80.5%)	128/119.8	
	High	86/91 (94.5%)	86/75.5	
Dukes B	Low	196/302 (64.9%)	196/218.2	(89.8)
	High	161/227 (70.9%)	161/186.6	(86.3%)
Dukes C (1 & 2)	Low	126/229 (55%)	126/218.8	(57.6%)
	High	103/225 (40.4%)	103/212	(48.6%)
Dukes C ₁	Low	107/252 (42.5%)	107/182.4	(58.6%)
	High	97/223 (43.5%)	97/184.9	(52.4%)
Dukes C ₁ (<5 nodes)	Low	93/205 (45.4%)	93/144.2	(64.5%)
	High	87/162 (53.7%)	87/132.1	(65.9%)
Dukes C ₁ (<5 nodes and upper two thirds rectum)	Low	64/147 (43.5%)	64/103.5	(61.8%)
	High	69/125 (55.2%)	69/101.6	(67.9%)
Dukes C ₂	Low	19/47 (40.4%)	19/36.4	(52.2%)
	High	6/32 (18.7%)	6/27.1	(22.2%)

NS—not significant.

laterally to the iliac nodes via lymphatics in the lateral ligaments.¹⁰ Also, low-lying rectal cancers can spread to the superficial inguinal nodes via lymphatics that run along the inferior rectal vessels.¹² In studying the subgroup of patients with Dukes' C₁ cancers of the middle and upper rectum having fewer than five metastatic nodes, we hoped to identify those who, because of limited proximal extent and minimal tendency to spread laterally, might theoretically be benefited by a high tie. Unfortunately, similar age-corrected 5-year survival rates in the low and high tie groups were obtained.

In a study such as this, it is likely that in both the Dukes C₁ and C₂ stages, the low and high tie groups are not identical. For example, the C₁ high tie group may contain some cases that would have been C₂ had a low tie been performed. Likewise, some C₂ low tie cases might have been C₁ if a high tie had been done, which may explain why the high tie C₂ patients survived less well than those in the low tie C₂ group. Furthermore, while most surgeons performing these operations tended to favor one type of ligation over the other, the possibility of some selection cannot be ruled out. Nevertheless, the numbers in the study are large and if high tie conferred a considerably improved survival, it would seem likely for this to have been evident.

In conclusion, high ligation of the inferior mesenteric artery has not been found to improve 5-year survival in patients with cancer of the rectum or rectosigmoid.

Acknowledgments

Our sincere thanks to Jill Grimsey for typing the manuscript, Kathy Clench for illustration, and Jill Maybee for photography.

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