

AN ANALYSIS OF 284 PATIENTS WITH PERFORATIVE CARCINOMA OF THE COLON

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CONSIDERING males and females together, carcinoma of the colon and rectum is the most common human cancer. Estimated cancer incidence rates for the United States in 1962, as reported by the American Cancer Society, comprise 72,000 cases of cancer of the large intestine surpassing carcinoma of the breast by approximately 9,000 cases. Since the majority of carcinomas of the large intestine are within reach of the proctoscope, this disease has been termed the most easily diagnosed internal cancer. It seems particularly unfortunate that the success rate in the treatment of this disease has not kept pace with the immense strides made in the technical performance of operative procedures, preoperative and postoperative care, and the acquisition of knowledge pertinent to the pathologic physiology and bacteriology of the large intestine. These factors have contributed conclusively to a reduction in operative mortality. There are perhaps 3 ways from which improvements in the cure rate can be expected to come. The first is prophylactic and concerns itself with removal of what many believe to be premalignant lesions of the large intestine: adenomatous polyps and villous adenomas. The second concerns itself with the extension and accentuation of simple diagnostic techniques already within the province of every physician and the final testing of more sophisticated maneuvers designed to increase the yield of early curable cancers. The third area of investigation currently being pursued

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is that of logical extension of standard operative procedures. One aspect of extended operations for lesions of the colon and rectum concerns those carcinomas that have undergone free perforation, frank abscess formation, fistulization into a neighboring hollow viscus, or have become densely adherent to an adjacent structure. These lesions have often been considered incurable.

Much has been written concerning the operative management of colonic cancer from the point of view of attacking the spread of the disease through lymphatic, venous, and intraluminal routes. However, relatively little has appeared in the literature regarding those lesions of the perforative type. In an attempt to ascertain whether a defeatist attitude is justifiable in this type of tumor, we have analyzed all lesions in these 4 perforative categories selected from 1,102 patients with carcinoma of the colon and rectum treated initially at the Hospital of the University of Pennsylvania from 1940 through 1956.

This group of 284 patients comprises approximately 26 per cent of all patients with carcinoma of the colon and rectum admitted during this time. In each patient the diagnosis of perforation was made or confirmed at laparotomy. All patients were followed up either to death or for a minimum period of 5 years from the date that operation was carried out.

ANATOMIC DISTRIBUTION OF TUMOR

The general distribution of the lesions in various portions of the colon follows the relative frequency of occurrence when all carci-

TABLE I.—ANATOMIC DIS

Location	Fixation
Rectum	99
Rectosigmoid	11
Sigmoid	46
Descending colon	17
Splenic flexure	6
Transverse colon	12
Hepatic flexure	6
Ascending colon	6
Cecum	10

TABLE II.—I

	No. of pa!
Fixation.....	213
Abscess.....	43
Fistula.....	21
Free perforation.....	7
Total.....	284

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TABLE I.—ANATOMIC DISTRIBUTION OF 284 COLONIC TUMORS AND THEIR RELATIONSHIP TO OVER-ALL 5 YEAR SURVIVAL

Location	No. of patients				Total		Over-all 5 year survival		
	Fixation	Abscess	Fistula	Free perforation	No.	Per cent	No.	Per cent	Gilbertsen all carcinomas
Rectum.....	99	8	6	1	114	40.1	17	14.9	26
Rectosigmoid.....	11	5	0	0	16	5.7	1	6.2	28
Sigmoid.....	46	11	7	1	65	22.9	24	36.9	33
Descending colon..	17	5	1	1	24	8.5	8	33.3	37
Splenic flexure....	6	3	1	1	11	3.9	3	27.2	8
Transverse colon..	12	0	3	1	16	5.6	10	62.5	46
Hepatic flexure....	6	3	1	0	10	3.5	3	30.0	31
Ascending colon....	6	1	0	1	8	2.8	1	12.5	33
Cecum.....	10	7	2	1	20	7.0	6	30.0	35

TABLE II.—RATE OF RESECTION, OPERATIVE MORTALITY, AND 5 YEAR SURVIVAL

	No. of patients	Resections		Operative mortality		5 year survival	
		No.	Per cent	No.	Per cent	No.	Per cent
Fixation.....	213	182		6		55	25.8
Abscess.....	43	39		4		11	25.6
Fistula.....	21	17		1		6	28.6
Free perforation	7	5		1		1	14.3
Total.....	284	243	85.6	12	4.2	73	25.7

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nomas of the colon are considered (Table I). The rectum is defined anatomically as the distal 12 centimeters of the large intestine, with the 3 centimeter area just proximal to the rectum arbitrarily considered to be the rectosigmoid.

OVER-ALL RESECTABILITY RATE, OPERATIVE MORTALITY, AND 5 YEAR SURVIVAL

The over-all rate of resection, operative mortality, and 5 year survival is shown in Table II. Resectability rates have increased with the advent of routine blood banking, advances in anesthesia, the more or less routine use of preoperative intestinal preparation, antibiotics, and the recognition on the part of surgeons that even a limited resection provides the only effective palliation in most patients. The rate of resection, 85.6 per cent, is comparable to the figures for all carcinomas of the colon cited by Welch and Burke. The over-all operative mortality rate was 4.2 per cent, highly acceptable in view of the fact that the operative mortality rate for colectomy for all reasons during the past decade at the Hospital of the University of Pennsylvania has been 3.6 per cent. The causes of the 12 postoperative deaths follow the pattern of operative deaths from extensive intra-abdominal operations with pulmonary embolus, peritonitis, and upper gas-

trointestinal hemorrhage comprising the majority of the complications. Lymph nodes were positive for carcinoma in 32 per cent of the total group. Eighteen per cent of patients exhibited distant metastases at the time of laparotomy. The over-all 5 year survival was 25.7 per cent, the patients with free perforations into the peritoneal cavity having the poorest prognosis. It is known that 7 patients living 5 years after resection later died of the colon cancer. The small number of late deaths, after 5 years, mirrors the experience of others who have noted the comparative rarity of this occurrence in contradistinction to carcinomas arising from the breast or thyroid. On the other hand, 16 patients who died less than 5 years after resection had no evidence of cancer either clinically or at autopsy. Therefore, the actual cure rate may be slightly higher than that which is recorded here.

It is to be noted that the 5 year survival rate is absolute survival, i.e., all patients alive after 5 years in comparison to all patients who entered the hospital with the disease, not excluding operative mortality. This appears to us to be the only relevant way of indicating the virulence of a given disease since it is possible in Moore's phrase, to "improve surgical results by really trying." Gilbertsen has pointed out that the apparent

improvement in survival from colon cancer is related to the use of selected patients in statistical analysis. An absolute 5 year survival rate of 32 per cent was reported by him in an analysis of 840 unselected patients with carcinoma of the colon. It is apparent from Table I that the survival rates for perforative lesions are comparable to, or better than, his figures for an unselected series, except for the rectum, rectosigmoid, and ascending colon. Grinnell (6) has also stated that the absolute 5 year survival rate for colon cancer is a little better than 25 per cent. The gross survival rate of 473 patients with carcinoma of the rectum and rectosigmoid at the Hospital of the University of Pennsylvania during the same time period that this present study represents was, again, only 25 per cent (12). In this latter group, if one included only the survival for patients with carcinoma believed to be curable at the time of operation, the figure would rise to 37 per cent. It is apparent from these data therefore that extension of a colonic lesion outside of the confines of the intestinal wall by no means presages incurability.

FIXATION TO ADJACENT STRUCTURES

The tumor was fixed to adjacent structures in 213 patients. Pathologic examination of the contact area, or site of attachment, was available in 73 instances. Inflammation and not carcinoma caused the fixation in the majority of instances, 54.8 per cent, in accord with previous studies. The organs secondarily involved by the tumor and the corresponding 5 year survival rates are indicated in Table III. When the tumor had become attached to the sacrum or anterior or posterior aspects of the abdominal wall, the 5 year survival was 23 per cent, similar to the 20 per cent figure reported by Merrill for patients surviving resection in whom the tumor had become adherent to the anterior aspect of the abdominal wall. Taylor and his associates found a 5 year salvage of 33 per cent in patients in whom the colonic lesion had attached itself to the urinary bladder, somewhat better than our

results of 21 per cent, although the number of patients is relatively small. In 5 out of 18 instances in which the carcinoma was adherent to the small intestine, a cure was attained. Moersch reported a 16.5 per cent survival rate in the 28 per cent of the 54 instances in which the tumor had become adherent to more than one structure or one organ.

It was possible to perform a primary or delayed resection in 85.6 per cent of patients. A primary resection was the rule. The overall operative mortality in this group was 2.8 per cent. The organ or structure involved by the tumor was resected in 40.4 per cent, and the tumor "peeled off" the involved structures in the remainder. If the adherent area was carcinomatous and was resected, the survival rate was not significantly different from the survival rate for the over-all group, which was 24.2 and 25.8 per cent, respectively.

Lymph nodes were positive for tumor in 37 per cent of the patients with resections. When the adherent area was due to the direct extension of the tumor, there was little change in this incidence, 39.4 per cent. Distant metastases existed in 20.7 per cent of the patients at the time of laparotomy.

An attempt to encompass the entire local extent of the disease with the coincident removal of a portion of an affixed organ is worthwhile in this group of patients. Colon cancers notoriously are surrounded by an inflammatory or desmoplastic area which accounts for the local fixation in over half of the patients. Probably the most common site for local recurrence of rectal carcinoma in the female is in the vaginal area and cul-de-sac. We have not hesitated to resect the adnexa, uterus, and a portion of the vagina, if this appears to have a significant effect on the individual patient's prognosis. In the male, the base of the bladder in the area of the ureters is commonly the site of residual tumor. A portion of the bladder can be sacrificed with impunity where it is adherent to the tumor and the patient still be provided with an adequate opportunity for cure.

It is noteworthy that in the transverse colon, with primary and proximal resection, the direct extension of the tumor is superior to the large intestine series and in our series. Fixation of the distal colon and this certain cure.

Without a doubt, with certainty the contact areas significant subsequent little over half of the tissue will be to us judicious absence of certainty, which, provided by excising the bounds of resection extended resectable with a mortality rate opportunities for

LOCALIZED PERFORATION

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It is noteworthy that lesions of the transverse colon, with its relatively short mesentery and proximity to other organs, do not have the dire prognosis that might be anticipated. In fact, the long term survival rate is superior to that in any other area of the large intestine in Gilbertsen's unselected series and in our own small group of adherent lesions. Fixation may occur at an earlier stage of the disease in the transverse colon, and this certainly is not incompatible with cure.

Without a controlled series we cannot state with certainty that resection en bloc of contact areas significantly influences the patient's subsequent course. Furthermore, in a little over half of the instances this adherent tissue will be benign. Nevertheless, it seems to us judicious to resect contact areas in the absence of certain knowledge of their benignancy, which, in any event, can only be provided by excision biopsy. If performed within the bounds of reasonable surgical judgment, extended resections of this type are compatible with a highly acceptable operative mortality rate and, very likely, added opportunities for cure.

LOCALIZED PERFORATION WITH ABSCESS FORMATION

The tumor had perforated locally with the formation of an abscess in 43 patients. Only those instances in which a frank purulent collection was present are included in this category. It was not considered sufficient if the lesion simply had an area of inflammatory reaction adjacent to it. None of these lesions involved the transverse colon. All but 5 of the patients underwent a primary resection with an over-all operative mortality of 9.3 per cent. Only 4 individuals had demonstrable distant metastases at the time of laparotomy, and lymph nodes were positive for tumor in less than a third. Examination of the abscess wall was performed in 23 instances, and carcinoma was found in 9. The over-all 5 year survival rate was 25.6 per cent but only 1 patient survived 5 years in the group in which carcinoma was found

TABLE III.—FIXATION AND ORGAN INVOLVED

Adherent organ	No. of patients	Per cent 5 year survival
Prostate.....	17	17.6
Sacrum, anterior or posterior abdominal wall.....	74	23
Bladder.....	19	21.1
Small intestine.....	18	27.8
Another portion of colon.....	7	42.9
Stomach.....	2	100
Ovary.....	4	25
Uterus.....	8	12.5
Liver.....	1	0
Gallbladder.....	2	50
Spleen.....	2	50
Diaphragm.....	1	0
Vagina.....	4	50
Multiple structures.....	54	27.8

upon pathologic examination of the abscess wall.

Our aggressive approach to this type of lesion is manifest in the number of patients subjected to primary resection. We are in general agreement with Crile, Donaldson, and others that an aggressive surgical attack on the source of contamination and the elimination of suppurative foci afford the patient the best chance for cure and a smoother postoperative course. If the disease is left in situ it produces further debility in a patient who has usually already been subjected to severe physiologic and metabolic derangements. As Donaldson has stated, "it is the disease and not the operation that most often causes death, and more attention should be paid to eradication of the disease." Since the vast majority of our patients underwent resection primarily, and since the operative mortality and 5 year survival are relatively acceptable, it is tempting to unite these two statements in a causative, rather than simply an associative manner. It is impossible, obviously, to extract from our data the end result had a preliminary diverting colostomy been performed in every patient, with or without surgical drainage of the abscess cavity. Abdominal drainage, however, has frequently been implicated as the cause for subsequent local abdominal wall recurrences. However, preliminary diversion of the fecal stream is sometimes necessary when the abscess is large, anatomic landmarks are obscured, and an adequate primary resection

TABLE IV.—ORGANS INVOLVED IN FISTULA FORMATION

Organ involved	No. of patients	No. of 5 year survivors
Stomach.....	2	2
Duodenum.....	1	—
Small intestine.....	4	—
Colon.....	7	2
Bladder.....	3	2
Bladder and vagina.....	1	—
Small intestine and colon.....	1	—
Vagina.....	2	—
Total.....	21	6

of mesenteric lymph channels is impossible. If this situation occurs in conjunction with a lesion in the right or transverse colon, we prefer an end-to-side ileocolostomy, providing complete diversion, in addition to the nutritional advantages accruing from refunctionalization of the intestinal tract. When the abscess is small and well localized, we believe that it should be resected at the time of the initial operation as part of an adequate curative procedure. The degree of peritoneal contamination determines the feasibility of primary anastomosis at this time. Peritoneal lavage is probably valuable as an adjunctive procedure. If, after resection of such a lesion on the left side of the colon, anastomosis is thought to be unwise, the proximal end can be brought out as an end-colostomy and the distal end either brought through the abdominal wall as a mucus fistula or oversewn, similar to a Hartmann procedure. After the inflammatory reaction subsides and the patient is believed to be free of recurrent tumor for a suitable period of time, re-establishment of the continuity of the fecal stream can be accomplished as a second stage.

FISTULA FORMATION

The tumor had perforated into a hollow viscus with the formation of a fistula in 21 patients, 6 of whom achieved 5 year survival. The organs involved and the respective survival data are shown in Table IV. The organ into which the tumor had penetrated was resected en bloc with the lesion in over half the resected patients, with 1 operative death. Examination of the site of the fistula

was performed in 11 instances, 9 of which revealed carcinoma. The survival rate for this small group with proved malignant fistulization was comparable to that for the total series.

In the vast majority of patients with colon cancer in which a communication has formed with another hollow viscus, the clinical situation allows for elective, careful preoperative evaluation and preparation. In line with observations of others, we have found that a barium enema more often reveals the site of the fistula than barium taken by mouth. It is almost always possible to resect a portion of all of the secondarily involved organ as part of an adequate cancer operation. Another portion of the colon was the organ most frequently involved in our series, requiring, on occasion, an expansion of the usual resection for carcinoma. Both patients with gastroduodenal fistulas from lesions of the transverse colon were apparently cured of their disease by partial gastrectomy in continuity with a colectomy. That carcinoma, rather than inflammation, was the predominant finding at the fistula site in this group adds credence to this type of surgical approach.

PERFORATION INTO THE FREE PERITONEAL CAVITY

These patients represent true surgical emergencies and compound the prior wasting effects of the malignant tumor with a considerable amount of peritoneal contamination. Seven patients are included in this category with only 1 long term survivor. Of the 5 patients in whom it was possible to perform a primary resection, 1 died within 30 days of operation.

Although our experience with this type of lesion is not large, we tend to concur with the opinion of others that the source of peritoneal contamination should be either resected or exteriorized. Again, this decision becomes a matter of fine surgical judgment and depends primarily on the over-all clinical evaluation of the patient, and the duration and extent of peritoneal insult. If these factors are favorable, then wide resection

usually without p strongly urged.

ASSOCIATED COLONIC

In the present series had either a second colon incidence of multiple the large intestine. associated adenoma in their course, age findings for colon reported by Grinn to view the adenoma "of a colon v neoplasia, either 'yps, or villous ad associates were una dence that benign: sition to carcinom vestigators showe and rectum occur quency in polyp I dividuals—10.4 v that "patients wit as likely to develo with a single pol by Enterline and pital of the Univ per cent of the ca associated adeno mas of the colo vanced are not ne increased numbe

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ASSOCIATED COLONIC CANCERS OR POLYPS

In the present series of 284 patients, 6 per cent had either a synchronous or metachro-
nous second colon cancer, similar to the in-
cidence of multiple lesions generally found in
the large intestine. Nineteen per cent had an
associated adenomatous polyp at some time
in their course, again similar to the clinical
findings for colon carcinoma of all types, as
reported by Grinnell and Lane (7). We tend
to view the adenomatous polyp as a "symp-
tom" of a colon which is prone to produce
neoplasia, either "frank cancer," other pol-
yps, or villous adenomas. Rider and his as-
sociates were unable to find conclusive evi-
dence that benign adenomas underwent tran-
sition to carcinoma. However, these same in-
vestigators showed that cancer of the colon
and rectum occurs "with 5 times greater fre-
quency in polyp patients than in normal in-
dividuals—10.4 versus 2.1 per cent" and also
that "patients with multiple polyps are twice
as likely to develop carcinomas as individuals
with a single polyp." In the series reported
by Enterline and his associates from the Hos-
pital of the University of Pennsylvania, 23
per cent of the carcinomas had one or more
associated adenomas. Apparently, carcino-
mas of the colon that are locally far ad-
vanced are not necessarily associated with an
increased number of these "sentinel polyps."

DISCUSSION

Whereas reports of a 50 per cent or more 5
year survival from the more favorable group
of colon cancers are common in the literature,
few fall into this group and probably not
much over one-quarter of all individuals in
the United States afflicted with this disease
survive 5 years. The recurrences which cause
the patient's death are often local rather than
metastatic, although many are mixed. Our
therapeutic efforts are a long way from sat-
isfying the hopes of most forward-looking sur-
geons. A portion of the failures must be as-
cribed to the abridgement of vigorous sur-

gical therapy because of a nihilistic attitude
toward certain types of colon lesions.

The statistics for the over-all incidence of
involved lymph nodes and distant metastases
in these patients with perforative lesions
are of considerable interest. In a retrospective
study of this type certain conclusions are haz-
ardous. However, it seems justifiable to state
that the 32 per cent of individuals who had
positive nodes is considerably less than the
usual incidence of 47 to 68 per cent, quoted
by several investigators. In a similar vein, an
18 per cent incidence of distant metastases at
the time of laparotomy in our series compares
favorably with the series of 600 patients re-
ported by Bacon and Jackson, 25.8 per cent
of whom had visceral metastases at the time
of surgical intervention. It seems possible to
us that these locally advanced carcinomas
may, in reality, be somewhat less virulent in
their capacities for widespread metastasis
than the usual malignant tumors of the large
intestine. This potentially practical point will
have to be definitively demonstrated by fu-
ture investigators. Local control of this par-
ticular disease then may provide an inroad
into a surgical problem which has too often
been handled inadequately, and seldom
treated with the aggressiveness it deserves.
Hopefully, an altered approach to the prob-
lem will provide many more individuals the
chance for elimination of their disease and
the ability to secure the maximum extension
of a useful life.

SUMMARY

The clinical findings in 284 patients with
perforative carcinoma of the colon have been
analyzed. These lesions should never be con-
sidered categorically inoperable. The resect-
ability and 5 year survival rates, the opera-
tive mortality, and the incidence of distant
metastases compare favorably with unse-
lected carcinomas of the colon. An aggressive
approach to such lesions appears warranted.

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COMPARATIVE HEALING IN

L. C. GETZEN, M.D.
C. K. HOLLOWAY

IT HAS BEEN STATED that the mucosa is left exposed in the cavity, fistulas or abscess formation was precluded. The works of Richerand who noticed that adhesions were formed when the lesions were copied that adhesions were intestinal wound healed, when the fewer adhesions were less than satisfactory.

We have observed evidence of fistulas appendiceal stump effort is made to control another study during were evaluated in was occasionally interference was found or 3 weeks postoperative suture-bearing. To evaluate mucosal function, gastrointestinal intentionally everted healing was observed was tested.

MATERIAL AND METHODS

In an attempt to achieve anastomosis, healthy rats were operated upon with a variety of procedures, with the

From the Surgical Research Laboratory, University of California, San Diego.
The opinions or assertions of the writers and are not necessarily the views of the Navy Department, or the