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Peritoneal Carcinomatosis from Adenocarcinoma of the Colon

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Abstract. Peritoneal carcinomatosis is a major cause of surgical treatment failure in patients with colorectal cancer. In the past patients with this condition have had a lethal outcome. In this study, 64 consecutive patients were treated by the cytoreductive approach, which involved surgery to maximally resect all cancer in the abdomen and pelvis, early postoperative intraperitoneal chemotherapy with 5-fluorouracil (5-FU) and mitomycin C, and three cycles of adjuvant intraperitoneal 5-FU with systemic mitomycin C. The clinical features that may affect prognosis were assessed and critically analyzed statistically. Peritoneal implant size of < 5 cm present in the abdomen and pelvis at the time of exploration correlated with a good prognosis ($p < 0.0001$), as did complete cytoreduction with tumor removed to nodules < 2.5 mm ($p < 0.0001$). Involvement of only one or two of the five abdominopelvic regions, compared to three or more regions, was a significant determinant of prognosis ($p < 0.0001$). Finally, a mucinous histologic type correlated adversely with prognosis when compared to intestinal-type adenocarcinomas ($p < 0.001$). These data suggest that patients with small-volume peritoneal seeding from colon cancer should be treated with cytoreductive surgery and aggressive regional and systemic chemotherapy in an attempt to achieve long-term disease-free survival.

Adenocarcinoma of the colon is one of the most common internal malignancies, affecting about 1 person in 20 in the United States and in Western countries [1]. The major anatomic sites for colorectal cancer dissemination include metastases to the lymph nodes, hematogenous metastases to the liver, and cancer spread to the resection site and peritoneal surfaces. Peritoneal dissemination of colon cancer cells is a common cause of morbidity and eventual mortality with recurrent disease that may result in intestinal obstruction, symptomatic ascites, and intestinal fistulization. Carcinomatosis from colon cancer is a clinical entity characterized by peritoneal implants of the tumor at the resection site, on the peritoneal surface, or most commonly at both of these anatomic locations. Peritoneal carcinomatosis has, to this point in time, been regarded as a lethal condition with a median survival of only approximately 9 months [2].

In an attempt to critically evaluate a treatment plan for patients with peritoneal carcinomatosis from colon cancer, 64 consecutive patients were studied prospectively. The new surgical treatment strategy utilized three components: (1) The goal of cytoreductive surgery was to achieve minimal disease-free margins of resection [3]. (2) Surgery was combined with early postoperative intraperitoneal chemotherapy. (3) Patients were given at least three cycles of delayed intraperitoneal and systemic chemotherapy [4–10]. Reported here is the experience with this disease treated by a uniform management plan over a period of 12 years.

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Patients and Methods

Patients

Between 1982 and 1994 a total of 64 consecutive patients with histologically proved peritoneal carcinomatosis from colonic cancer were treated. This population represents the complete experience with this treatment plan, with no patients eliminated from the data analysis. There were 38 men and 26 women, ranging in age from 24 to 83 years (median 51 years). The median follow-up was 12 months (range 0.3–140.0 months). No patients were lost to follow-up. The preoperative workup was aimed at quantitative evaluation of the abdominopelvic disease, ruling out extraabdominal dissemination. Clinical examination and laboratory tests included carcinoembryonic antigen (CEA) lung assay, computed tomography (CT) scans, abdominal and pelvic CT scans, and appropriate upper gastrointestinal series or barium enema radiographs. Patients with liver or lymph node metastases in addition to peritoneal carcinomatosis, as determined by preoperative abdominopelvic CT scan, were not treated by this protocol unless it was thought that all cancer at these distant sites could be resected. Only those with a small peripheral liver metastasis on CT scan that could be removed by a wedge excision were considered for treatment. Patients with lymph node involvement along the aorta, vena cava, or in the celiac group were not treated. Pathology reports and slides from prior surgical procedures were reviewed to confirm the diagnosis of peritoneal carcinomatosis in all patients.

Cytoreductive Surgery

The goal of surgical treatment in these patients with peritoneal carcinomatosis from colon cancer was to remove, if possible, all clinical evidence of disease. A planned electrosurgical approach

Table 1. Clinical features analyzed in patients with peritoneal carcinomatosis from colon cancer.

Features not significant
Age
Sex
Grade
Location primary (right vs. left)
Ascites (present vs. absent)
Prior chemotherapy
No. of prior surgical procedures
Preoperative CEA (< 5 ng vs. > 5 ng)
Postoperative CEA (< 5 ng vs. > 5 ng)
Postoperative complications
Free interval (< 1 year vs. > 1 year)
Lymph node and liver metastases
Induction chemotherapy
Significant features
Lesion size
Abdominal regions involved
Histologic type (adenocarcinoma vs. mucinous adenocarcinoma)
Completeness of cytoreduction

for the removal of as much disease as possible required the use of one to six peritonectomy procedures plus appropriate intestinal resections. The cytoreductive surgery is described elsewhere [3, 11].

Intraperitoneal Chemotherapy

The rationale for intraperitoneal drug administration in patients with peritoneal carcinomatosis was established by pharmacologic studies [5–7, 12, 13]. Intraperitoneal chemotherapy was considered to have incomplete access to all peritoneal surfaces and limited penetration into tumor nodules that were contacted. Therefore to destroy a maximal volume of tumor over a unit of time, the intraperitoneal chemotherapy was applied after as complete cytoreduction as possible. Maximum effects from regional drug delivery were expected only if the tumor itself was bathed by the chemotherapy agents.

To gain maximal distribution of the intraperitoneal chemotherapy to all abdominal surfaces, drug installations were begun during the early postoperative period before wound healing closed off some peritoneal surfaces by an adhesive process. Therefore after completing the cytoreductive surgical procedure and prior to closing the abdominal cavity, a Tenckhoff catheter was placed through the abdominal wall for chemotherapy installation. Closed suction drains were placed underneath the diaphragm and in the pelvis to drain fluid from the abdomen. Immediately after closure of the abdominal incision, in order to keep the tubes and drains clear, repeated abdominal lavage with 1.5% dextrose dialysate was initiated to remove blood products and tissue debris that resulted from surgery.

On postoperative day 1, mitomycin at 10 to 12 mg/m^2 in 1000 ml of 1.5% dextrose peritoneal dialysis solution was instilled by gravity drainage. On postoperative days 2 to 5, we instilled 5-fluorouracil (5-FU) at 15 mg/kg in 1000 ml of dialysis fluid buffered with sodium bicarbonate at 50 mEq/L. Drugs were allowed to remain in place for 23 hours and were removed by the closed suction drains over a period of 1 hour. On the sixth postoperative day, all fluid was drained from the peritoneal cavity, and the Tenckhoff catheter was withdrawn from its tract; the closed suction drains were removed as surgically indicated.

Table 2. Summary of significant clinical features.

Clinical feature	No. of patients	5-Year survival (%)	p
Cytoreduction			
Complete	36	37	0.0001
Incomplete	28	0	
Lesion size			
0 to ≤ 5 cm	17	68	0.0001
> 5 cm	47	4	
Distribution			
One or two abdominal regions	29	48	0.0001
$\geq$ Three abdominal regions	35	4	
Histopathology			
Intestinal type	23	44	0.0120
Mucinous	41	9	

Twelve patients selected because the peritoneal seeding had a small lesion size received three cycles of intraperitoneal chemotherapy preoperatively. This induction was an attempt to simplify cytoreductive surgery through a reduction of tumor volume on small bowel surfaces [14]. The remainder of the patients received adjuvant intraperitoneal 5-FU and systemic mitomycin [15]. All 64 patients received a total of four cycles of intraperitoneal chemotherapy unless complications, postoperative death, or early recurrence made it impossible.

Data Analysis

The clinical features selected for analysis of prognosis were sex, age, pre-resection lesion size, grade of tumor, lymph node and liver metastases, location of primary tumor (right colon versus left colon), presence of ascites, use of induction chemotherapy, prior chemotherapy, extent of prior surgery, CEA preoperatively, CEA baseline postoperatively, abdominopelvic regions involved, histologic type (adenocarcinoma versus mucinous adenocarcinoma), completeness of cytoreduction, postoperative complications, and free interval (Table 1). The clinical significance of each of these clinical features was analyzed. A Kaplan-Meier survival curve was fitted to the data and tested using a log rank test for difference between curves. The response variable was survival in months for clinical features itemized in Table 2. The p values were calculated for each analysis.

Assessment of Preoperative Lesion Size

Prior to resection and after thorough exploration of the abdomen and pelvis, the lesion size of peritoneal implants was assessed. Excluded from the lesion size analysis were major tumor masses at the resection site or at anastomoses that could be included in an en bloc resection. An absence of tumor seen at the time of operation in patients receiving induction chemotherapy was classified as lesion size 0. Minimal implant size was designated lesion size 1 with nodules < 0.5 cm. Lesion size 2 indicated moderate-size tumor nodules (0.5–5.0 cm), and lesion size 3 indicated large nodules (> 5 cm). A matting of structures together by tumor at any site that was not resectable with clear margins was classified as lesion size 3. The distribution of the implants throughout the abdomen and pelvis did not influence the lesion size. It should be

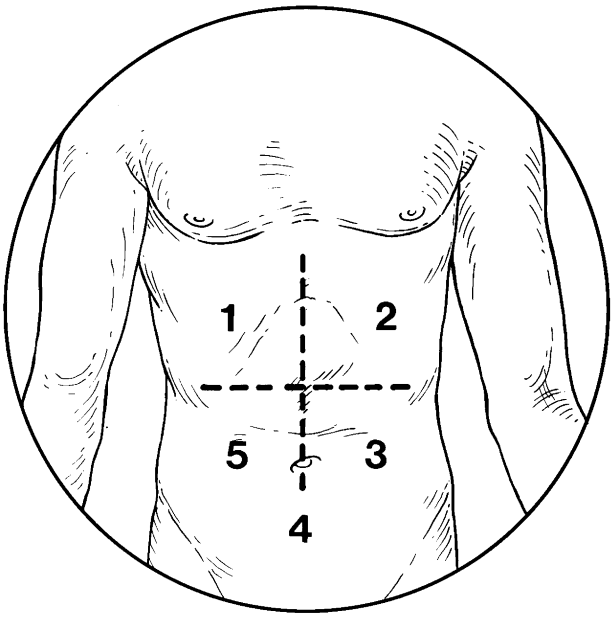

Fig. 1. Distribution of cancer within the peritoneal cavity.

emphasized that the lesion size assessment concerned carcinomatosis, so a large resectable tumor mass was not used to determine the lesion size.

Abdominopelvic Regions Involved

The abdominopelvic cavity was divided into five regions that included the four abdominal quadrants plus the pelvis (Fig. 1). This assessment, which allowed quantitation of the distribution of peritoneal carcinomatosis, was performed as part of the thorough exploration of the abdomen prior to cytoreduction. It was designed to answer the question, "How widespread is the disease?" If only one abdominopelvic region was involved, it was considered to be minimal involvement; involvement of two regions was considered to be moderate; and three or more regions with tumor nodules was considered to be extensive tumor involvement.

Tumor Histology

The histologic type of peritoneal carcinomatosis from colonic cancer was determined from a review of the surgical specimens pre- and postoperatively to exhibit no changes over time. Mucinous adenocarcinoma had a cytologic appearance similar to that of adenocarcinoma but differed in that there was abundant extracellular mucus. Almost all adenocarcinomas produce some mucin; mucinous tumors were those with an unusually large amount of mucin production. Symonds and Vickery classified tumors as mucinous if $> 60\%$ of the surface area of microscopic sections was occupied by mucus, and the same convention was followed here [16].

Completeness of Cytoreduction

The completeness of cytoreductive surgery was assessed by the operating surgeon at the conclusion of the cancer resection. A CC-0 resection meant that no tumor was seen free in the peritoneal cavity at time of operation: There was an en bloc resection of tumor with no known tumor contamination of peritoneal surfaces. Also, patients in whom there was a complete response to induction of chemotherapy were scored CC-0. A CC-1 resection meant that visible tumor left behind in the abdomen or pelvis was < 0.25 cm in diameter. A CC-2 resection indicated that after cytoreduction there were visible tumor nodules > 0.25 cm and < 2.5 cm in greatest diameter left behind. A CC-3 resection designated residual tumor nodules > 2.5 cm. A continuous surface of tumor remaining behind after cytoreductive surgery indicated a CC-3 assessment even though the surface was of minimal thickness.

Grading

The colonic adenocarcinoma specimens of intestinal type or mucinous type were divided into three grades based on established pathologic criteria. For grade 1 lesions there was minimal atypia of the individual tumor cells, and with mucinous tumors there were single or small clusters of tumor floating in colloid. For grade 2 cancers there was some stratification of cells on a fibrous stroma. Atypia was present, but an organoid morphology was preserved. Grade 3 carcinoma showed solid areas of cancer with necrosis present. Atypia was prominent, and mitotic activity was present. Upon examination of adjacent normal tissues, invasion into fat, muscle, or bowel wall was noted. Grade 3 malignancy included all signet ring adenocarcinomas. Grading was performed for both the primary cancer specimen whenever slides for review were available and for cancer removed by cytoreduction.

Results

Overall Survival

The median survival of these 64 patients was 11.9 months. At the time of preparation of this manuscript 23% of patients were alive with no evidence of disease, 16% of patients were alive with disease, 59% of patients died of disease, and 2% of patients died of other causes.

Analysis and Pre-resection Lesion Size

In three patients no tumor was seen at the time of operation; all three of these patients had undergone induction chemotherapy prior to cytoreductive surgery. None of the patients had lesion size 1 (nodules < 0.5 cm); 14 patients had tumor nodules of 0.5 to 5.0 cm; and 47 patients had a large lesion size (nodules > 5 cm). The 5-year survival rate was 68% for the 17 patients with no tumor seen or with lesion size 2. Only 4% of patients with lesion size 3 survived 5 years. There is statistical significance between these groups ($p = 0.0001$). Figure 2 shows the survival analysis for no lesion to moderate lesion size preoperatively versus large lesion size.

Analysis of Involvement of Abdominopelvic Regions

An estimate of localized versus widespread distribution of cancer was obtained using the assessment illustrated in Figure 1. Among

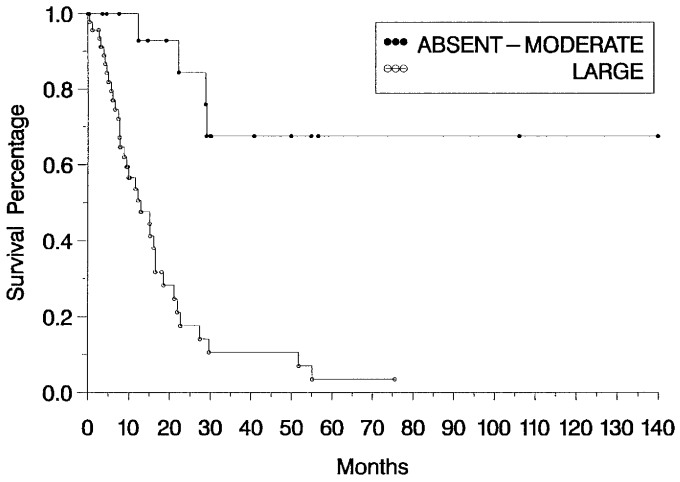

Fig. 2. Survival by analysis of pre-resection lesion size.

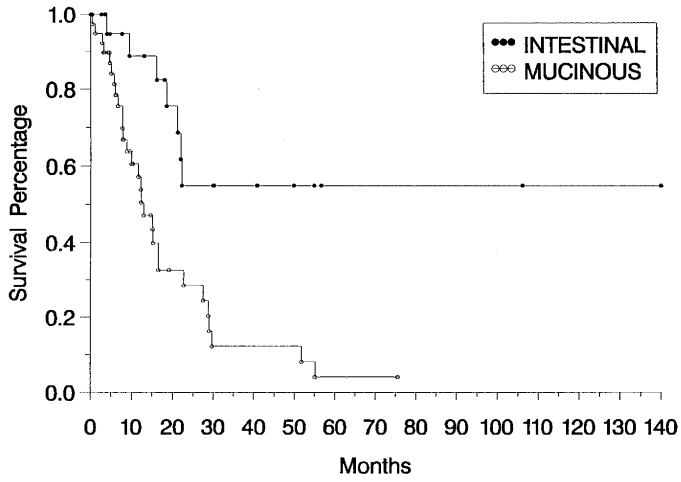

Fig. 4. Survival by analysis of histopathologic type.

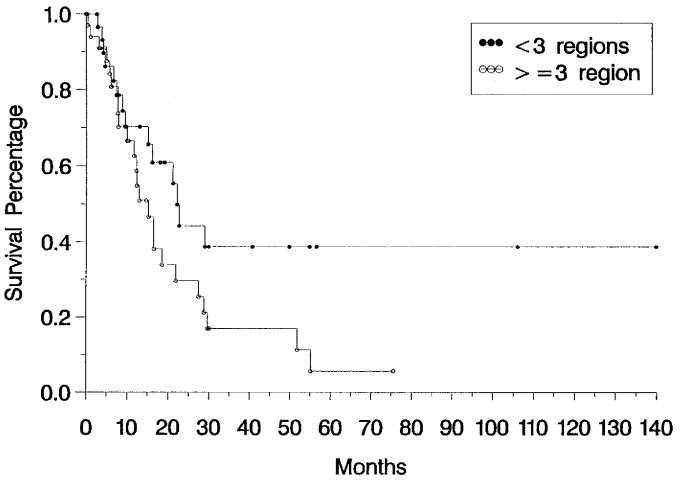

Fig. 3. Survival by analysis of distribution of peritoneal carcinomatosis.

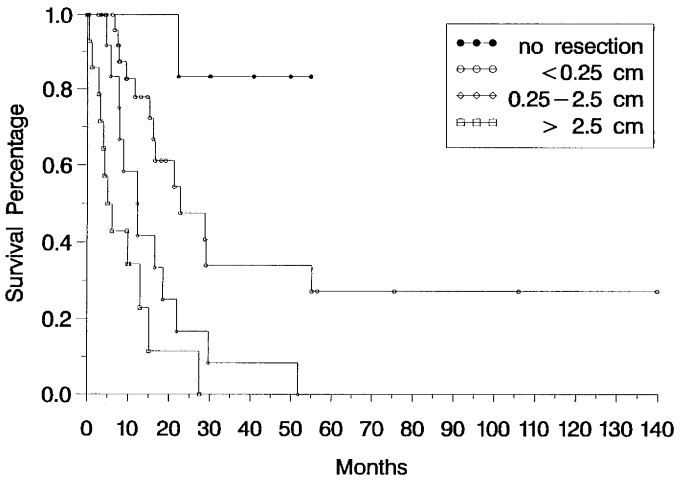

Fig. 5. Survival by analysis of completeness of cytoreduction.

the patients, 9 had one region involved, 17 had two regions involved, and 35 had three or more regions involved. As illustrated in Figure 3, patients with one or two abdominopelvic regions involved had a statistically superior survival than those with three or more regions involved ($p = 0.0001$).

Analysis of Histologic Type

Twenty-three patients were identified as having intestinal-type colonic adenocarcinoma and forty-one as having mucinous adenocarcinoma (Fig. 4). The survival of those with intestinal-type adenocarcinoma was better than that of patients with mucinous adenocarcinoma; the analysis was statistically significant ($p = 0.0120$). Greater lesion size preoperatively and more involved abdominal regions may be responsible for this result. Patients with mucinous adenocarcinoma had larger lesions than adenocarcinoma patients ($p = 0.001$). Also on average they involved 2.8 abdominal regions, whereas the adenocarcinoma lesions involved an average of 1.5 regions ($p = 0.0001$).

Analysis of Completeness of Cytoreduction

Of 64 resections, 7 were classified as CC-0. Of 64 cytoreductions, 29 were considered complete (CC-1). The 5-year survival for complete cytoreduction (CC-0 and CC-1) was 37%. Patients with CC-2 or CC-3 scores after cytoreduction were considered to have had incomplete cytoreductions, and the overall 5-year survival rate for the incomplete cytoreduction group was zero. Figure 5 shows the survival for completeness of cytoreduction for the four groups (0–3). There is a statistically significant difference between these groups ($p = 0.0001$).

Analysis of Lymph Node or Liver Metastases in Patients with Peritoneal Carcinomatosis

A total of 23 peritoneal carcinomatosis patients in this study had no evidence of lymph node or liver metastases at any time during their treatment. This analysis was based on a negative pathology report and intraoperative assessment at the time of resection of the primary colon cancer and at the time of cytoreductive surgery.

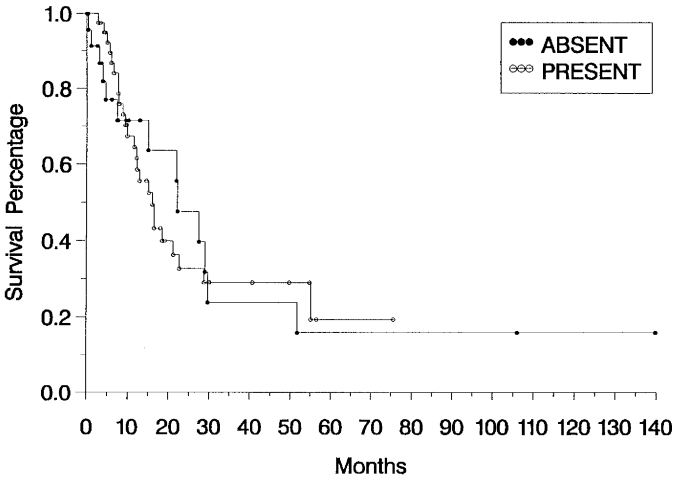

Fig. 6. Survival by analysis of the absence versus the presence of resectable lymph node or liver metastases.

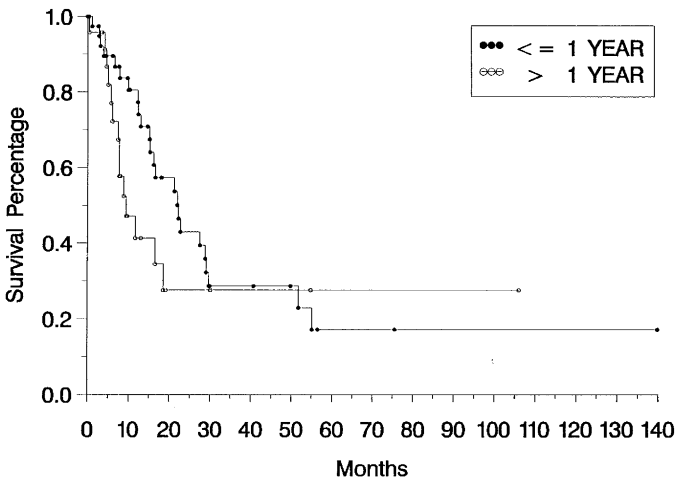

Fig. 7. Survival by analysis of free interval of less than 1 year versus 1 year or more.

Of course, later development of lymph node, liver, or other distant metastasis during follow-up for these treatments would not indicate metastases present in this analysis. Figure 6 shows the survival of peritoneal carcinomatosis patients with or without other sites of potential resectable disease. There is no significant difference in survival.

Survival by Free Interval

An important consideration when selecting patients for resection of metastatic disease from colon cancer has been determined to be the interval between the resection of the primary cancer and the resection of the metastasis [17, 18]. In these patients with peritoneal carcinomatosis the survival of patients with a free interval of < 1 year was compared to those with a free interval of ≥ 1 year. Figure 7 shows that there was no difference in survival for these two groups of patients.

Analysis of Sex and Age

Male patients accounted for 59% (38/64) and female patients for 41% (26/64). The overall survival rate for 5 years is 17% for men and 16% for women. The median age is 51 years (range 24–83 years). There is no statistically significant difference in survival between the men and women or by age of < 40 years versus ≥ 40 years.

Analysis of Grade

Only 2 of 64 patients (3%) had low grade tumors, whereas 32 patients (50%) had a grade 2 tumor and 30 patients (47%) had a high grade tumor. The survival rate was nil in the group of patients with grade 1 tumor, 30% in the group with grade 2 tumor, and 12% in the group of patients with grade 3 tumor. These differences are not statistically significant.

Analysis of Complications After Surgery

The incidence of complications after cytoreductive surgery and early postoperative intraperitoneal surgery was 23.2%. These complications have been described extensively in other publications [19–23]. The survival rate for the patients with no complications was 30.7% and for patients with complications 30.2%. There was no statistical difference between these two groups.

Sites of Treatment Failure

The anatomic sites of treatment failure were determined for 36 patients who died of disease or who are alive with disease. All except one of these 36 patients had progression of disease on peritoneal surfaces. Of the 36 patients with recurrence, 19 (52.8%) developed only local recurrence. Four patients developed local and pleural recurrence. Eight patients had local recurrence and lung metastases. One patient developed local recurrence and lymph node metastases. Three patients developed local recurrence with lymph node, liver, and lung metastases. One patient developed liver and lung metastases with no local recurrence.

Discussion

The original efforts to treat peritoneal carcinomatosis definitively by surgery plus intraperitoneal chemotherapy were in patients with ovarian cancer. Assessments of these efforts were not favorable [24]. Peritoneal carcinomatosis treatments for appendiceal cancer have met with greater success [4, 6, 23–25]. Selection of patients with mucinous tumors of low biologic aggressiveness and complete cytoreduction were the determinant variables [25]. Limited success with the treatment of peritoneal implants from gastric cancer has also been reported [26–28]; heated intraoperative intraperitoneal mitomycin and cisplatin were used for these treatments. The present study is the first that reports success in the management of peritoneal carcinomatosis from colon cancer. It also is the initial effort to analyze the clinical features of these patients so proper patient selection can benefit future patients. These prognostic features can exclude patients unlikely to benefit from therapy and bring about an improvement in the results of the patients who are treated.

These data suggest that pre-resection lesion size of peritoneal implants and tumor distribution are clinical determinants that can be used to select patients most likely to benefit from the cytore-

ductive approach if they are explored for peritoneal carcinomatosis from colon cancer. Unfortunately, these assessments are not made until the abdomen has been widely opened. Better preoperative assessments of the volume and distribution of cancer in patients with peritoneal carcinomatosis should be sought and would assist with the selection of patients for treatment. The work of Jacquet and colleagues show that the CT scan is a poor radiologic test for accurate assessment of peritoneal carcinomatosis [29]. CT scans with intraperitoneal contrast provide little additional information [30]. Others suggest that laparoscopy preoperatively may help one select patients with small-volume disease. Because of adhesions from prior surgical procedures, however, laparoscopy is not a definitive test in many patients. Better preoperative evaluations of peritoneal carcinomatosis patients must be sought.

Another important factor—unfortunately dependent on preresection lesion size and distribution—is the completeness of the cytoreduction. A complete cytoreduction was possible in 36 patients, meaning that no visible tumor > 0.25 cm was left behind in the abdomen after the cytoreductive surgery. After receiving their early postoperative and adjuvant intraperitoneal chemotherapy, 39% of these patients were alive at 5 years. The results suggest that this treatment strategy is most appropriate in patients in whom it is possible to achieve complete cytoreduction. A debulking procedure in which gross cancer was left behind after surgery was not associated with long-term survival.

From these data one may have hope that long-term survival in patients with peritoneal carcinomatosis from adenocarcinoma of the colon is possible. Nearly 40% of patients with complete cytoreduction were alive at 5 years. The strategy suggests that aggressive treatment is appropriate in patients with minimal implant size and limited intraperitoneal dissemination. If local control of small-volume disease within the peritoneal cavity is achieved by cytoreductive surgery and early postoperative intraperitoneal chemotherapy, the quantity and quality of life may be improved for these patients.

To improve the results of this treatment it may be worthwhile to combine cytoreductive surgery with heated intraoperative intraperitoneal chemotherapy, as has been done for gastric cancer [26–28]. Heated chemotherapy solutions may facilitate penetration of drug into large tumor nodules. Data regarding this hypothesis are currently being gathered.

It may seem strange that mucinous adenocarcinoma patients would have a worse prognosis than patients with adenocarcinoma. However, the volume of mucinous adenocarcinoma was larger, as assessed at the time of surgery ($p < 0.001$). Also, the distribution of cancer was more widespread with mucinous adenocarcinoma (mean 2.8 regions involved compared to 1.5 regions). Mucinous tumors produce a mucous ascites that facilitates movement of cancer cells around the peritoneal cavity [25], which results in widespread tumor underneath the hemidiaphragms and within the pelvis. This cancer can be stripped away in patients with pseudomyxoma peritonei, but this removal is less likely to be accomplished with invasive malignancy [3].

Some contradictions with previous reports are apparent when the data on colon cancer are compared to those for appendiceal cancer. With peritoneal carcinomatosis from grade 1 mucinous adenocarcinoma (pseudomyxoma peritonei), the volume of disease documented within the abdomen preoperatively did not correlate with improved survival or disease-free survival [23]. Even bulky pseudomyxoma peritonei patients have an excellent prognosis with the cytoreductive approach. The difference in prognosis for large-volume colon cancer versus large-volume appendiceal malignancy lies in the invasive character of the two malignancies. Even though there is extensive pseudomyxoma peritonei spread diffusely throughout the abdominal cavity, peritonectomy procedures can achieve complete cytoreduction, and intraperitoneal chemotherapy can control the growth of minimal residual disease so these surgical gains are not lost over time.

These data together suggest that some changes in the management of patients with colon and rectal cancer are required. Approximately 10% of these patients have peritoneal seeding at the time of their primary cancer [1]. Other patients have bowel perforation through the primary tumor, adjacent organ invasion, or positive peritoneal cytology, suggesting a high likelihood of future development of peritoneal seeding. Also patients who are diagnosed with small-volume peritoneal seeding at the time of reoperative surgery may be treatable for cure. The patients with low-volume, minimally distributed carcinomatosis are ideal candidates for the cytoreductive approach.

Our current strategy involves patients with limited intraperitoneal cancer volume. Three cycles of induction intraperitoneal 5-FU plus systemic mitomycin are given. After a 2-month interval, the patient is again explored, all residual cancer is removed by resection or peritonectomy, and intraperitoneal chemotherapy is given. The mitomycin is given intraoperatively with 42°C heat and continuous manual distribution of chemotherapy to all abdominal and pelvic surfaces. The 5-FU is given intraperitoneally during the first 5 postoperative days with frequent turning of patients to gravity distribute the chemotherapy. These refinements in the cytoreductive approach and its limited application to a selected group of patients may improve the results of treatment of peritoneal carcinomatosis.

Résumé

La carcinose péritonéale est une cause majeure d'échec du traitement chirurgical chez les patients ayant un cancer colorectal. Autrefois, la carcinose péritonéale était considérée comme un arrêt de mort certain. Dans cette étude, nous avons traité 64 patients consécutifs avec une approche dite «cytoréductive». Cette technique comporte une résection maximum de tout le tissu cancéreux dans l'abdomen ou dans le pelvis, une chimiothérapie intrapéritonéale précoce utilisant le 5-FU et la mitomycine C, puis trois cycles de chimiothérapie systémique de 5 FU combiné avec de la mitomycine C. On a analysé les caractéristiques cliniques pouvant influencer le pronostic. Une taille de nodule inférieure à 5 cm au niveau de l'abdomen ou du pelvis au moment de l'exploration est corrélé avec un bon pronostic ($p < 0.0001$). La cytoréduction complète combinée avec l'ablation de tous les nodules de moins de 2,5 cm était corrélée avec un bon pronostic ($p < 0.0001$). Le pronostic était encore favorable lorsque seulement une ou deux des cinq régions abdomino-pelviennes étaient intéressées. Par contre, le type mucineux était de mauvais pronostic en comparaison avec le type adénocarcinomateux ($p < 0.001$). Ces données suggèrent que le patient avec des nodules péritonéauxde petite taille provenant d'un cancer colique devrait être traités par la chirurgie cytoréductive et une chimiothérapie régionale et systémique agressives afin d'obtenir une survive à long terme sans récidive.

Resumen

La carcinomatosis peritoneal es una causa mayor de falla del tratamiento quirúrgico en pacientes con cáncer colo-rectal, quienes en el pasado exhibían una evolución fatal. En el presente estudio se estudiaron 64 pacientes tratados mediante el método de citorreducción. El método consiste en cirugía para lograr una máxima resección del cáncer en el abdomen y la pelvis, quimioterapia intraperitoneal precoz con 5-FU y mitomicina C, y tres ciclos de quimioterapia intraperitoneal adyuvante con 5-FU y mitomicina C por vía sistémica. Se evaluaron las características clínicas que pueden afectar el pronóstico, las cuales fueron sometidas a análisis estadístico. Un tamaño < 5 cm de los implantes peritoneales en el abdomen o la pelvis en el momento de la exploración apareció correlacionado con un buen pronóstico ($p < 0.0001$). Una completa citorreducción con remoción del tumor hasta nódulos de < 2.5 mm apareció correlacionada con buen pronóstico ($p < 0.0001$). La invasión de sólo 1 o 2 de las cinco regiones abdomino-pélvicas en comparación con 3 o más regiones apareció como un factor significativo de pronóstico ($p < 0.0001$). Finalmente, el tipo histológico mucinoide exhibió correlación inversa con el pronóstico, en comparación con los adenocarcinomas de tipo intestinal ($p < 0.0001$). Estos datos, tomados en conjunto, sugieren que los pacientes con cáncer de colon y con siembras peritoneales de pequeño volumen deben ser tratados con cirugía citorreductiva y quimioterapia local y sistémica agresiva, con el propósito de lograr sobrevidas libres de enfermedad a largo plazo.

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Invited Commentary

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Unfortunately, solid tumors arising from abdominal organs are classified as those resistant to anticancer drugs. Colon cancer especially shows low response after chemotherapy, and surgery is the only treatment that offers hope of cure. Peritoneal dissemination from colon cancer is observed in 5% to 10% of all cases, and this type of metastasis has been considered difficult to treat by surgery or chemotherapy. The reasons for such difficulties are as follows: (1) incomplete resection of the peritoneal dissemination only by surgery; and (2) low penetration of the systemically infused drugs into the abdominal cavity [1, 2].

During the last few years, several methods, such as intraperitoneal chemohyperthermia [3], neoadjuvant chemotherapy [4], and aggressive cytoreduction of the peritoneal dissemination [5] have been developed and reported. Because the effects of chemotherapy are inversely related to tumor burden, intraperitoneal chemotherapy immediately after aggressive cytoreduction may achieve long-term survival. In this sense, the strategy of Sugarbaker et al., consisting of maximal cytoreduction and early postoperative intraperitoneal chemotherapy, is logical. Furthermore, their quantification of the degree and distribution of the peritoneal dissemination is unique and readily available. I recommend that every surgeon use their criteria and that the survival curves of each group or the effects after chemotherapy be compared using this classification.

We have reported that intraoperative chemohyperthermia is effective for the peritoneal dissemination from gastric cancer [6]. Furthermore, we proposed a new surgical procedure called peritonectomy [6]: While performing a peritonectomy, parietal peritoneum and almost all the peritoneum bearing peritoneal seeding are stripped away, and all the macroscopically observable tumors are maximally resected. The final goal is a condition of no macroscopic residual disease in the abdominal cavity. For patients with gastric cancer, total gastrectomy, splenectomy, and subtotal colectomy were performed. For patients with colon cancer, the whole stomach is preserved but the omental bursa including the greater omentum is resected in combination with subtotal colectomy. After peritonectomy, intraoperative chemohyperthermia using heated saline at 43°C containing mitomycin C, etoposide, and cisplatinum is applied for 60 minutes. Eleven patients with peritoneal dissemination were treated with this new therapy: two had colon cancer and nine had gastric cancer. Ten patients are alive now, and the 1-year survival rate is 100%. The longest survivor is alive 4 years after the procedure without recurrence.

From the results of Sugabaker et al. and our experience, it can be concluded that combination therapy with aggressive cytoreductive surgery and subsequent intraperitoneal chemotherapy may effectively achieve long-term survival of patients with peritoneal dissemination. Physicians should thus change their treatment policy regarding peritoneal dissemination.

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