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Pseudomyxoma Peritonei

Long-Term Patient Survival with an Aggressive Regional Approach

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Objective
The aims of this study were to analyze the natural history of patients with pseudomyxoma peritonei (PMP), evaluate clinical and pathologic variables as prognostic indicators, and review the authors' experience with different treatments.

Summary Background Data
PMP is an unusual form of intra-abdominal neoplasm that presents with large amounts of extracellular mucin. Diffuse peritoneal spread occurs in most patients with PMP, and distant metastasis is infrequent. Debulking surgery, radiation therapy (radioisotope and external beam), and chemotherapy (both intraperitoneal and systemic) have all been advocated for optional patient management, but the variability of patients studied, the small patient numbers, and the prolonged course of this disease make the evaluation of results difficult.

Methods
Fifty-six patients were treated for PMP at the Mayo Clinic between 1957 and 1983. The data were collected retrospectively. Univariate (log-rank test) and multivariate (Cox regression model) analyses were performed for disease recurrence and patient survival.

Results
Most patients with PMP had carcinomas of the appendix (52%) or ovary (34%). All gross tumor could be removed only in the 34% of patients with limited disease. Although tumor progression occurred in 76% of patients, the 1-, 5-, and 10-year survival rates were 98%, 53%, and 32%, respectively. Adverse predictors of patient survival included weight loss ($p = 0.001$), abdominal distention ($p = 0.004$), use of systemic chemotherapy ($p = 0.005$), diffuse disease ($p = 0.038$), and invasion of other organs ($p = 0.04$). Intraperitoneal chemotherapy ($p = 0.009$) and radioisotopes ($p = 0.0043$) both were effective in prolonging the recurrence time of symptomatic PMP.

Conclusions
Although PMP is an indolent disease, aggressive surgical debulking followed by intraperitoneal radioisotopes and/or chemotherapy should be considered because of the diffuse peritoneal involvement.

Pseudomyxoma peritonei (PMP) is a rare clinical condition characterized by large collections of mucin in the abdomen. This condition was originally described in association with benign ovarian cystadenoma[1] and benign appendiceal mucocele.[2] Although these benign causes have been included in many reports,[3-6] present consensus would suggest that PMP be reserved to describe those patients with an abdominal carcinoma.[7-11]

Appendiceal and ovarian cancers give rise to the majority of cases, but there are reports of PMP occurring in association with pancreatic carcinoma,[12,13] carcinoma of the breast,[14] and bile duct cancer.[15] The majority of PMPs occur in association with low-grade carcinomas,[11] which may account for the frequently observed indolent course of this disease. Metastasis is an extremely rare event,[11,16] and death is usually the result of extrinsic intestinal obstruction by tumor masses.

Because of the loose terminology applied to this condition in the literature, the paucity of reported cases, and the variable or prolonged course of the disease, reliable indices for prognosis are unavailable, and the optimal treatment is difficult to evaluate. Many authors believe that radical and repetitive "debulking surgery" should form the mainstay of palliative treatment.[5,6,17,18] Others strongly suggest that adjuvant intraperitoneal[19,20] or systemic chemotherapy[11] confers additional benefit and may, in certain patients, be curative.[11,19-21] Adjuvant radiation therapy also has its proponents.[11] In sharp contrast, there are those who believe that equally good survival rates may be attained by avoiding surgical intervention.[22]

Until the natural history of this entity can be more accurately defined and parameters can be chosen that might earmark those patients in need of aggressive therapy, progress will, by necessity, be slow. This review was undertaken to analyze our experience with a large group of patients who presented with the clinical syndrome of PMP and had documented intra-abdominal carcinomas. The aims of this study were to analyze the natural history of the disease, examine the clinical and pathologic features that might act as prognostic indicators, and review our experience with available therapeutic modalities.

MATERIALS AND METHODS

Subjects

The records of 56 consecutive patients who presented to the Mayo Clinic in the 26-year period between 1957 to 1983 were analyzed retrospectively. Complete follow-up was achieved in 55 (98%) of the patients (one patient was lost to follow up after 9 years). All patients had initial and subsequent surgical treatment at the Mayo Clinic. Data were retrieved in regard to patient presentation, the origin of the tumor, the type of initial surgical procedure, the histologic type, adjuvant therapy, the timing and type of recurrence, further treatment, and survival.

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Methods

All pathologic materials were reviewed by a single pathologist (J.R.G.) to confirm the original diagnoses. Adequate archival pathologic specimens were available from 37 patients (20 with appendiceal carcinoma, 16 with ovarian tumors, and 1 from a tumor of uncertain primary) and processed for flow cytometric analysis. Control ovarian and appendiceal specimens (ten of each) were obtained from patients undergoing oophorectomy for benign disease or incidental appendectomy. Sections were obtained to prove histologically the nature of malignant (patients) or nonmalignant (controls) tissues.

Nuclear suspensions were prepared from the paraffin-embedded tissue blocks using the technique of Ryan et al.,[23] a modification of the technique of Hedley et al.[24] The isolated nuclei were stained with propidium iodine according to the method of Rainwater et al.,[25] a modified technique from that originally described by Vindelov et al.[26]

The nuclear DNA content was quantified on a FACS IV flow cytometer (Becton-Dickinson, Mountain View, CA) (according to the method of Ryan et al.[23]) and classified as one of three nuclear DNA ploidy patterns: normal (diploid), tetraploid/polypoid, or aneuploid. The tumor DNA content was classified as "aneuploid" when a peak distinct from both the normal G0/G1 (2C) and smaller G2/M (4C) peaks was present. For aneuploid tumors, a DNA index was calculated as the ratio of the peak channel of the abnormal DNA stemline of cells to the peak channel of the DNA normal cells. When the Fullbright fluorosphere single peak was set at channel 35, the Fullbright fluorosphere doublet peak appeared at channel 76; thus, the ratio of singlet to doublet peaks was 2.17. The mean (± standard deviation) coefficient of variation of the G0/G1 peak was 8.2 ± 2.6. A nuclear DNA content histogram classified as "tetraploid/polypoid" had a 4C peak that was significantly increased over that present for the DNA normal (diploid) pattern. The cutoff between the normal and abnormal percentages of nuclei in the 4C peak was arbitrarily set at three standard deviations above the mean 4C percentage present in the control specimens.

Statistical Methods

Information on both patient survival and tumor recurrence were described using Kaplan–Meier methods. Pa-

Table 1. PRESENTING SYMPTOMS

Symptom	Percentage of Patients
Pain	52
Abdominal distension	44
Anorexia and nausea	11
Weight loss	9
Vomiting	7
Fatigue	4
Urinary symptoms	4
Diarrhea	4

Table 3. INITIAL SURGICAL PROCEDURE

Procedure	Percentage of Patients
Appendectomy	61
Oophorectomy	41
Single	34
Bilateral	7
Omentectomy	38
Hysterectomy	27
Resection of other organs	2

tients with residual disease after the initial treatment were excluded from the analysis of recurrence. The data from patients who died without a recurrence were considered as censored observations at the time of death for recurrence. Univariate assessments of potential risk factors with respect to both recurrence and survival were based on the log-rank test for categoric variables. Multivariate analysis was performed using a forward stepwise Cox regression model with the addition of univariate variables with $p \leq 0.05$. All tests were two tailed.

RESULTS

Patient Presentation

There was a preponderance of women (64%), the mean patient age at presentation was 53.9 years (range, 17 to 79 years), and the median duration of symptoms was 2 months (range, 0 to 4.6 years). The presenting symptoms were most frequently abdominal pain and abdominal distention (Table 1). The most common findings on presentation were abdominal mass and abdominal distention (Table 2). The majority of cases were diagnosed surgically. During the review period, ultrasonography (US) and computed tomography (CT) were not routinely available for the evaluation of abdominal masses. In patients in whom radiologic investigations were performed at the initial presentation, an intra-abdominal mass was suggested by abdominal films in 8 of 23 (35%), gastrointestinal series in 11 of 23 (48%), and CT in 1 of 3 (33%). More recently, CT was found to be particularly helpful for preoperative assessment of tumor spread.

Table 2. PHYSICAL FINDINGS AND LABORATORY DATA AT PRESENTATION

Abnormality	Percentage of Patients
Abdominal mass	60
Gross abdominal distension	41
Fever	22
White cell count >10,000/mm^3	20
Peritoneal irritation	15
Hemoglobin <10 g/dL	5

Operative Findings

During surgery, the extent of disease was classified as diffuse in 61%, confined to the pelvis or one quadrant of the abdomen in 16%, and localized in 18% of patients. The extent of disease was unclassifiable in 5%. During the initial surgical procedure, an appendectomy (61%) or oophorectomy(s) (41%) was usually undertaken, with an additional organ resection when indicated, and attempted debulking of all mucus and peritoneal tumor (Table 3). Removal of gross disease and mucus was considered complete only in patients in whom disease was localized or confined to one abdominal quadrant or the pelvis (34% of patients). In those patients in whom the malignancy was diffuse or unclassified, subtotal debulking of the gross tumor was achieved in a further 60%. In the rest of the patients (6%), only a biopsy or bypass was performed.

Pathologic Findings

The site of tumor origin was most commonly the appendix (52%) or the ovary (36%), but the colon (4%), endometrium (2%), and pancreas (2%) were also involved. In three patients (5%), the organ of origin could not be determined. Tumor involvement of intra-abdominal organs besides the organ of origin occurred in 64% of patients. At initial presentation, 64% of patients had adenocarcinomas, 32% had cystadenocarcinomas, and 4% had unclassifiable tumors. These two patients at the time of subsequent disease recurrence had adenocarcinoma of the appendix and cystadenocarcinoma of the ovary. One patient with an intra-abdominal adenocarcinoma had a history of appendiceal mucocele resected elsewhere 5 years previously. The carcinomas were considered grade 1 in 87% and grade 2 in 9%. They were not graded in

4%. Nodal involvement or distant metastases were not observed.

Nuclear DNA Ploidy Patterns

Of the 37 carcinoma specimens available for flow cytometric analysis, 23 (62%) had a normal (diploid) nuclear DNA content, 6 (16%) were aneuploid, 2 (5%) were tetraploid/polyploid, and 6 (16%) could not be classified. All patients with cystadenocarcinomas had diploid tumors, whereas adenocarcinomas were either diploid (48%) or nondiploid (52%). There was no correlation between nuclear DNA ploidy and histologic grade.

Adjuvant Therapy

Intracavitary radiotherapy was used after surgery as treatment in 22% of patients and external beam irradiation, in 6%. Intracavitary therapy consisted of intraperitoneal ^{32}P in ten patients and ^{198}Au in two patients. Intraperitoneal or systemic chemotherapy was administered in 13% and 27% of patients, respectively, and most commonly consisted of 5-fluorouracil (5-FU) or cyclophosphamide instillations for intracavitary therapy or 5-FU, cyclophosphamide, L-phenylalanine mustard or doxorubicin as postoperative systemic chemotherapy. Mucolytic therapy was not given to any patient.

Disease Recurrence

The median patient follow-up for the entire group was 12 years (range, 9 to 25.6 years). In keeping with the expected clinical course of PMP, disease recurrence was noted in 38 of 50 patients (76%). In six patients who had progressive disease after minimal clearance, the tumor was termed "residual" rather than "recurrent." Within 2.5 years of initial surgery, 50% of the recurrences had been detected. There was no significant difference in the rates of recurrence between those patients with potentially curative resections (21 patients with localized disease) and those 28 patients who had subtotal debulking of diffuse tumor (76% *vs.* 75%, $p = 0.69$), although recurrences were symptomatic at a shorter postoperative interval in those with diffuse disease (*i.e.*, 50% of patients with diffuse disease had evidence of recurrence within 1.9 years *vs.* 2.6 years for localized disease). Follow-up physical examination was the most common method for the detection of tumor recurrence (Table 4).

The treatment of patients with persistent or recurrent disease involved surgery in the majority (71% of the 38 patients). Although the goal for operative treatment was total removal of the tumor, this was achieved in only 20%. In the remaining patients, subtotal mucus removal was performed in 53%, biopsy only in 20%, and palliative bypass or resection in 7%.

Table 4. PRESENTATION OF RECURRENT DISEASE

Means of Detection	No. of Patients (%)
Physical examination	14 (33)
Pain	6 (14)
Bowel obstruction	5 (12)
Laparotomy	4 (7)
Planned "second look"	3
Incidental	1
Gastrointestinal fistula	2 (5)
Cecal	1
Small bowel	1
Miscellaneous	7 (13)
Vaginal symptoms	2
Gastric outlet obstruction	1
Mass on abdominal x-ray	1
Unspecified	3

The histologic examination of recurrent disease differed from the initial examination in 23% of patients. Two converted from an unclassified malignancy to adenocarcinoma and cystadenocarcinoma, as previously described. In the remainder, progression from grade 1 to grade 2 carcinoma was noted in five patients, and one patient whose condition had initially been diagnosed as appendiceal adenocarcinoma presented with a new primary ovarian carcinoma.

Adjuvant radiotherapy was used in 29% of patients with recurrent malignancy (18% intracavitary radioisotope and 11% external beam), and 53% received chemotherapy (11% intraperitoneal). The chemotherapy drugs most frequently used were 5-FU, cyclophosphamide, and L-phenylalanine mustard.

Additional Disease Recurrences

Surgery for second recurrence was performed in 24 patients (67% of surviving patients with symptomatic recurrence) and was of a similar nature to that for the first recurrence. Removal or resection of all gross disease was performed in 13% of those patients with a second recurrence, subtotal mucus removal in 42%, palliative resection or bypass 4%, and biopsy only in 8%. The tumor pathologic type was different from that found during the initial operation in 17% of cases, generally with progression to a more undifferentiated carcinoma. Radiation therapy was used in 21% of patients (13% intracavity and 8% external beam); 42% received chemotherapy (29% intraperitoneal and 13% systemic). There were further recurrences in 15 patients (54% of surviving patients), and these patients were treated with further debulking surgery ($n = 12$), chemotherapy, and radiation therapy, as before.

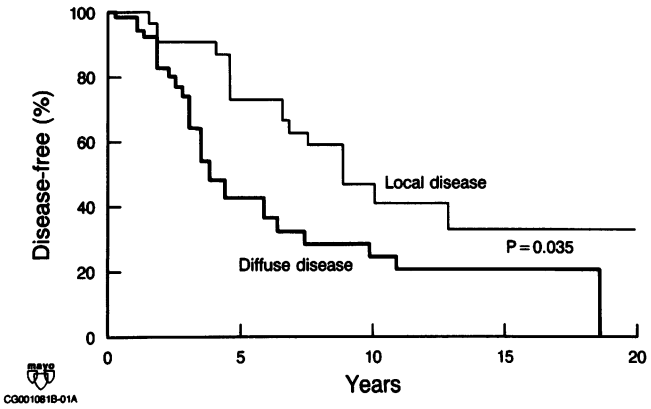

Figure 1. Effect of disease pattern (local, n = 21; diffuse, n = 34) on the disease-free interval.

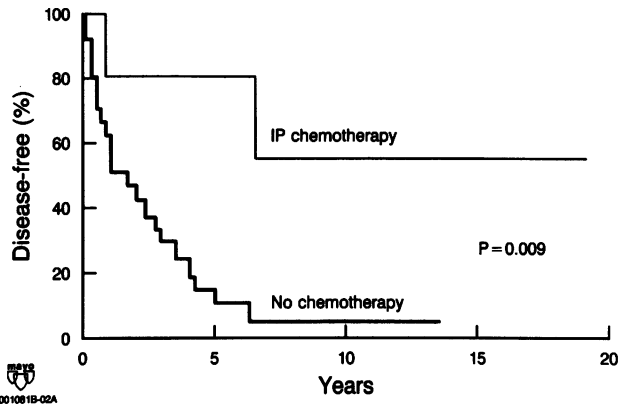

Figure 3. Effect of intraperitoneal chemotherapy (n = 5) *vs.* no intraperitoneal chemotherapy (n = 26) on disease-free intervals in patients with incomplete surgical removal of mucus.

Factors Affecting Disease Recurrence

An analysis of those factors that appeared to influence the recurrence rate indicated that the presence of abdominal distention (p = 0.006) and the lack of radioisotopic treatment (p = 0.004) were univariately associated with a shorter disease-free interval. Those patients with diffuse intra-abdominal disease had significantly higher rates of recurrence (p = 0.034, Fig. 1). In addition, there was a trend, although not statistically significant, for intraperitoneal chemotherapy to result in a longer disease-free interval (p = 0.059). The tumor's DNA content had no effect on the disease-free interval. In the subgroup of patients whose mucus removal was incomplete, instillation of a radioisotope (Fig. 2) or chemotherapy (Fig. 3) resulted in significantly lower rates of disease recurrence.

In a stepwise multivariate model, the lack of intracavitary radiation (p = 0.004), the presence of peritoneal signs on the initial presentation (p = 0.024), and incomplete mucus removal (p = 0.008) were associated with a significantly shorter disease-free interval. The patient's age and sex, the organ of origin, pain, the duration of symptoms, the extent of disease, the invasion of other organs, the histologic type or grade, and the tumor's DNA ploidy had no demonstrable effect on disease recurrence in the multivariate analysis.

Patient Survival

The median survival after surgery of this patient population was 5.9 years (range, 0.3 to 25.6 years; fig. 4). The estimated 1-, 2-, 5-, and 10-year survival rates were 98%, 86%, 53%, and 32%, respectively. Of those patients included in the study, 14 are alive and well, 1 patient is alive with disease, 35 patients died of PMP, 4 patients died without apparent disease, and 2 patients died of unknown causes. One patient, who was alive and free of clinical disease 9 years after surgery was the only subject lost to follow-up.

Factors Affecting Patient Survival

Those patients with diffuse disease had shorter overall survival times than did those with localized tumors (me-

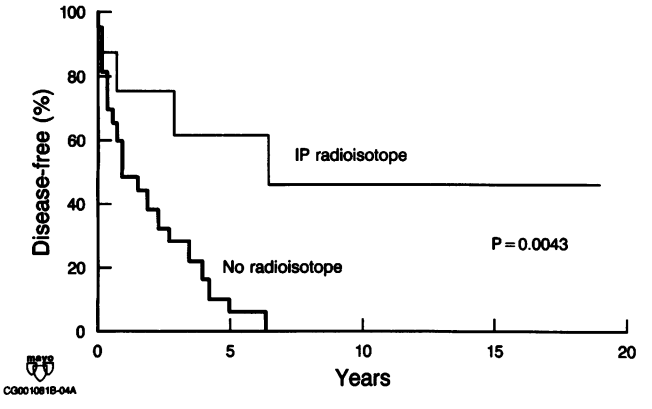

Figure 2. Effect of intraperitoneal instillation of a radioisotope (n = 8) *vs.* no radioisotopic treatment (n = 23) on disease-free intervals in patients with incomplete surgical removal of mucus.

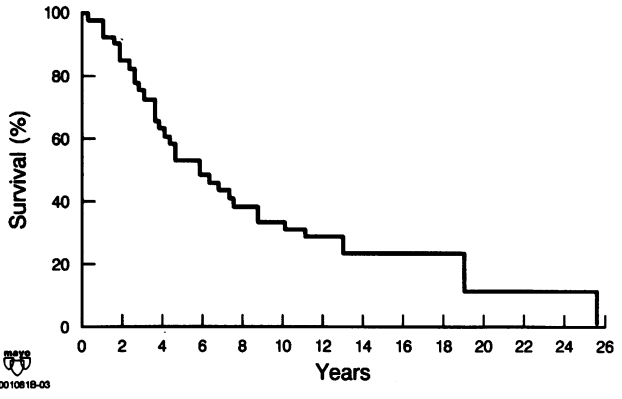

Figure 4. Kaplan–Meier survival curve for all patients with PMP.

Table 5. FACTORS ADVERSELY AFFECTING SURVIVAL BASED ON UNIVARIATE ASSESSMENT

Variable	p Value
Weight loss	0.001
Abdominal distension	0.004
Systemic chemotherapy	0.005
Incomplete mucus removal	0.010
Diffuse disease	0.036
Involvement of adjacent organs	0.038

dian. 3.8 *vs.* 8.4 years, respectively, p = 0.01). The presence of abdominal distention, a history of weight loss, the presence of diffuse disease or invasion of other organs, and postoperative systemic chemotherapy were associated with shorter survival times, using univariate analysis (Table 5). Women had a borderline improvement in survival compared with men (p = 0.05). There was a trend, although not statistically significant, for longer patient survival times when intracavitary radioisotopic treatment was given (p = 0.068).

A stepwise multivariate model demonstrated that only the use of systemic chemotherapy had a significantly adverse effect on patient survival. The histologic type and grade, the organ of origin, the tumor's DNA ploidy, the patient's age or gender, and the duration of symptoms had no demonstrable effect on patient outcome in multivariate analysis.

DISCUSSION

First described by Werth[1] in 1884 in association with a benign ovarian cystadenoma, the definition of PMP has been the subject of much confusion and varied interpretation in the literature. It is now generally agreed that the term PMP should be restricted to describe the condition of those patients in whom peritoneal mucus is found in the presence of an intraperitoneal adenocarcinoma.[7-11,19] Unfortunately, many reports of patients with PMP included large numbers of patients with appendiceal and ovarian mucoceles and cystadenomas.[3-6,18,27] Information in regard to patient survival and disease recurrence from such studies is misleading for PMP. In the present study, all patients had carcinoma with intraperitoneal mucinous deposits.

This present study reports the largest group of patients with PMP treated at a single institution. All surviving patients had a minimum follow-up of 9 years. As suggested in previous studies, PMP generally follows an unremitting but prolonged clinical course. The majority of our patients had recurrent disease despite aggressive surgery and the frequent use of radiation and chemotherapy. Despite the tenacity of the disease, patient survival times were prolonged compared with those seen with other forms of peritoneal carcinomatosis.

There have been reports of US[28] and CT,[29] which demonstrate characteristic radiologic findings of PMP. Our preoperative radiologic investigations were generally not helpful because most patients in this study were treated before the routine use of CT, US, or magnetic resonance imaging. Others reported similar findings,[11] although this situation has changed. More recently, we found that CT and US were invaluable in the preoperative assessment of PMP. Others suggest that magnetic resonance imaging may also be helpful in treating PMP.[30]

Histologic examination in our experience showed most malignancies to be low-grade carcinomas (86% were grade 1). This may account for the indolent behavior, lack of distant metastases, and frequent long-term survival associated with PMP. Distant metastases were not observed in any of our patients, although there have been isolated reports of metastases to vertebrae,[11] the chest cavity,[16] and lymph nodes.[21] It was suggested that PMP does not invade neighboring organs,[11,31] but some authors reported the invasion of adjacent abdominal organs.[32] In our patients, 65% had tumors with secondary organ invasion. Thus, the low-grade nature of the tumor may limit distant spread but allow local invasion, albeit at a superficial level.

In the recent literature, DNA ploidy was suggested to be a marker of metastatic potential[23,33] and a prognostic indicator for some neoplasms. DNA ploidy was not correlated with patient survival, disease-free interval, or histologic grade. However, data were available for only 67% of patients. Larger studies are indicated to determine whether DNA ploidy and other pathologic characteristics predict more aggressive or persistent forms of PMP.

In two large previously reported series of PMP, the survival rates at 5 years were 14% in a 1952 report from the Mayo Clinic[17] and 54% from the M. D. Anderson Cancer Center, as reported in 1980.[11] The latter figure closely compares with our current experience (53%) in a demographically similar group (64% women and a mean patient age of 53 years in our study compared with 65% and 54 years in the earlier study[11]). The 10-year patient survival rate for our group was better than that from the M. D. Anderson Cancer Center (34% *vs.* 18%). Better patient outcome was reported in smaller studies with shorter follow-up times (*i.e.*, a 70% 5-year actuarial survival rate in a group of 17 patients with appendiceal pseudomyxoma followed for a minimum of 5 years at Memorial Sloan-Kettering by Smith et al.[31]). Sugarbaker et al.[19] described patient "cures" after aggressive surgery with vigorous cauterization, multiple intraperitoneal infusions of chemotherapy, and regular follow-up laparotomies, but the median patient follow-up was less than 3 years. In this last study, there was a significant incidence

of complications, including a 21% rate of postoperative peritonitis, and most patients experienced major fluid shifts secondary to peritoneal injury after extensive electrocautery use.

It has been argued that surgical debulking of PMP should be performed on a selective basis, if at all,[21] because the mortality rates after extensive debulking surgery may be high.[34] In addition, patients have survived for 15 years or more without surgical intervention.[21] The basis for such arguments is far from sound. First, Friedland et al.[22] base their approach on the observation of a single patient in whom no histologic type was available (*i.e.*, a patient who refused surgery). It is possible that this patient had mucinous ascites secondary to a benign condition. Furthermore, the report of Little et al.[35] included patients with benign diseases. Finally, the patient survival rates we achieved with aggressive and repetitive surgical debulking with adjuvant therapy are outstanding (28% at 12 years) and without perioperative mortality (98% 1-year survival rates).

At our institution, the more frequent use of adjuvant therapy during the past few decades and a more aggressive surgical approach[17] may be responsible for the improvement in survival time compared with those in previous reports. Patient selection may also be a major factor because the earlier Mayo Clinic report[17] was confined to pseudomyxomas of ovarian origin and included more grade 2 carcinomas (more than 20%) than did the present study (8%).

Supporting the impression that more intensive management of this disease has improved patient outcome, intracavitary radiation was associated with longer disease-free intervals in the present study. This suggests that patients with PMP should receive radioactive phosphorus or some form of intracavitary radiotherapy, particularly if mucus removal is incomplete after debulking surgery. The trend toward improved survival rates after intracavitary radioisotopic treatment might attain significance with a longer follow-up or larger patient numbers. Fernandez and Daly[11] also suggested that radiotherapy may be a useful adjunct and noted an improvement in the 5-year survival rate from 44% for patients receiving chemotherapy to 75% for patients receiving radiation. Their patient numbers and follow-up, however, were too small and too short, respectively, to be statistically conclusive.

Systemic chemotherapy has been used in the treatment of PMP for many years. Despite the long experience with chemotherapeutic agents, there is no consensus whether such treatment is effective in this condition. There are anecdotal reports that suggest cure,[11,21] but it must be noted that, in one instance,[21] the ovarian histologic type was "borderline malignancy." More recently, investigators recommended that systemic chemotherapy be withheld for the treatment of PMP recurrence.[25] The failure to achieve objective responses with systemic chemotherapy may be related to the low grade of the tumor so often encountered in PMP or to the difficulty in characterizing a response after debulking surgery. The hypovascularity of the tumor and the bulk of residual disease in PMP adds to the difficulty of achieving high tumor concentrations of systemically administered chemotherapeutic drugs without profound toxicity.

Intraperitoneal chemotherapy previously was used in the treatment of PMP. The rationales for this treatment include: (1) extremely high and sustained levels of cytotoxic chemotherapeutic agents can be achieved in the abdomen,[36] (2) the water-soluble mucus cannot metabolize chemotherapeutic agents in the peritoneal cavity,[37] and (3) PMP superficially invades intra-abdominal organs and rarely metastasizes, allowing maximum exposure to the drug for a long period.[19] Our results suggest that the use of systemic chemotherapy had an adverse impact on patient survival, perhaps because of selection bias. By contrast, there was a trend toward improved survival rates in those patients who received intraperitoneal chemotherapy and a significantly reduced risk of tumor recurrence in those in whom debulking of mucus was incomplete. This trend toward improved survival rates with the use of intraperitoneal chemotherapy and the beneficial effect on tumor recurrence is comparable to the results of Sugarbaker et al.[20]

Patients with PMP are best treated with aggressive local therapy, a philosophy shared by other authors.[11,19,20] Although we advocate extensive surgical debulking of the tumor, the extremely aggressive approach of Sugarbaker et al.[19,20] entails a significant morbidity rate and has not yet shown better long-term survival rates than our more moderate approach. With our more conservative surgical excision of the tumor, patient survival rates at 2 and 5 years were 86% and 53%, respectively. Although five of the seven patients who had completed treatment were disease free at 2 to 4 years in the studies of Sugarbaker et al.,[19,20] longer follow-up is necessary before embracing this more toxic treatment regimen.

In conclusion, the findings in this report on 56 patients with PMP were similar to those in the limited available literature. PMP is a tenacious and indolent process, but with aggressive surgical debulking, long-term patient survival is possible. We recommend aggressive and repetitive "debulking" surgery for PMP, including appendectomy, bilateral oophorectomy, and omentectomy, at the initial procedure. Those patients who present with peritoneal irritation and a palpable abdominal mass, in addition to those with extensive and invasive disease, are most at risk for recurrence. These patients should be considered for additional therapy. From our experience and that of others,[11] intraperitoneal radioisotope instillation and chemotherapy seem to confer a disease-free survival benefit without increased rates of complications. The

value of prescribing systemic chemotherapy is less compelling, and this form of treatment should be withheld for the management of recurrent disease. Intraoperative phototherapy,[38] mucolytic therapy,[39] and other local regional treatments, used in conjunction with extirpative surgery, may be useful to treat patients with PMP in the future. The rarity of PMP and the long follow-up required to determine any survival advantage will continue to hamper the evaluation of results from any interventional trials.

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