

Cytoreduction including total gastrectomy for pseudomyxoma peritonei

P. H. Sugarbaker

Washington Cancer Institute, 110 Irving Street NW, Washington, DC 20010, USA

Correspondence to: Dr P. H. Sugarbaker (e-mail: Paul.Sugarbaker@medstar.net)

Background: Cytoreductive surgery supplemented by perioperative intraperitoneal chemotherapy is a therapeutic option for selected patients with pseudomyxoma peritonei syndrome. In some patients, the stomach and/or its vascular supply are so covered by mucinous tumour that total gastrectomy is required for complete resection.

Methods: Forty-five patients underwent total gastrectomy with a temporary diverting jejunostomy as part of the surgical treatment of pseudomyxoma peritonei syndrome of appendiceal origin. Heated intraoperative intraperitoneal chemotherapy with mitomycin was used in all patients, and 36 had early postoperative intraperitoneal 5-fluorouracil. To date, 39 patients have had second-look surgery and stoma closure; 37 had additional perioperative intraperitoneal chemotherapy. A prospective database was maintained on all patients.

Results: The median age was 47 (range 33–66) years. Median interval from diagnosis of pseudomyxoma peritonei to definitive cytoreductive surgery was 23 (range 0–140) months. Six patients presented with intestinal obstruction. The need for gastrectomy was predicted before operation by abdominal computed tomography. Mean operative time was 13 (range 9–17) h. Mean intraoperative requirement for packed red blood cells was 3.0 units, and that for fresh frozen plasma was 9.9 units. Six peritonectomy procedures, including total gastrectomy, were required for complete cytoreduction. All except seven patients were maintained on parenteral nutrition before second-look surgery for jejunostomy closure. All but two patients have resumed oral nutrition with discontinuation of parenteral feeding. There was one postoperative death and one late death. Thirty-seven patients are alive and disease-free, 0–56 months after initiation of treatment.

Conclusion: Total gastrectomy with a temporary diverting jejunostomy may be used to facilitate complete cytoreduction in patients with advanced pseudomyxoma peritonei syndrome.

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Introduction

The progression of peritoneal surface malignancy displays a predictable pattern of disease distribution throughout the abdomen and pelvis¹. In an aggressive malignancy such as intestinal-type colon cancer the peritoneal implants are distributed randomly on peritoneal surfaces near to the primary cancer. The surface of the primary tumour, greater omentum and paracolic gutters contain the majority of implants. In minimally invasive mucinous tumours coming from a perforated appendix, the predominant mass of peritoneal implants is redistributed by the flow of peritoneal fluid to dependent sites (pelvis and right retrohepatic space) and to sites of peritoneal fluid resorption (greater omentum and right hemidiaphragm)^{2,3}. Mobile surfaces such as the small bowel and its mesentery

may be completely free from tumour. This observation encouraged extensive parietal peritoneal and visceral resections with near-complete preservation of small bowel. In some patients with pseudomyxoma peritonei, complete cytoreduction requires peritonectomy, combined with total gastrectomy. To prevent the progression of microscopic residual disease the peritoneal space is treated intraoperatively and early after operation with intraperitoneal chemotherapy^{4,5}.

In the past, pseudomyxoma peritonei has been managed by serial debulking procedures. Gough and colleagues⁶ reported a median disease-free survival of 18 months, and only a few patients remained disease-free at 5 years. Improved results of treatment have become apparent as complete cytoreduction was attempted and intraperitoneal chemotherapy was used^{7–11}. Other groups have not accepted the profound impact of aggressive treatment on

survival and suggest that outcomes depend on histopathological subgroups of the disease¹².

With a complete parietal peritonectomy a prolonged paralytic ileus is observed; the small bowel may fail to move bile and other enteric contents by peristalsis for 2–3 weeks. Prolonged enteric drainage of the small bowel is necessary to decompress the gut and thereby allow suture lines, especially an oesophagojejunal anastomosis, to heal safely. Nasojejunal tubes do not allow adequate drainage of enteric contents. In a previous study of eight patients who had gastrectomy, duodenostomy tubes were used but caused a high incidence of complications; the most common complication was enteric leakage around the duodenostomy tube insertion site¹³. Furthermore, if the duodenostomy tube failed to function properly the oesophagojejunal anastomosis disrupted.

In the past, five different peritonectomy procedures have been reported: anterolateral peritonectomy (greater omentectomy–splenectomy plus stripping of paracolic gutters), left subphrenic peritonectomy, right subphrenic peritonectomy, cholecystectomy–lesser omentectomy plus stripping of the omental bursa, and pelvic peritonectomy with rectosigmoid resection¹⁴. When total gastrectomy is added as a sixth peritonectomy the requirement for reliable prolonged enteric decompression is evident. In this clinical situation a temporary diverting jejunostomy has been used in 45 patients to protect the oesophagojejunal anastomosis. The diverting stoma was closed 3–6 months later at the time of second-look surgery. The purpose of this manuscript is to present an experience of total gastrectomy and diverting jejunostomy in patients with pseudomyxoma peritonei syndrome who required total gastrectomy for complete cytoreduction.

Patients and methods

Over a 14-year interval, 381 patients with pseudomyxoma peritonei syndrome from a perforated appendiceal tumour had a complete cytoreduction. This was defined as removal of all visible tumour down to nodules 2.5 mm or less in diameter. In October 1996 a new approach to cytoreductive surgery in patients with large-volume perigastric disease was formulated. Since this time all patients requiring complete cytoreduction have been managed using this approach. The clinical data on 45 patients who had total gastrectomy with a temporary diverting jejunostomy are the focus of this study.

Surgical technique

In this approach to complete cytoreduction, the stomach and the majority of the parietal and visceral peritoneum were resected. The majority of the small bowel was

preserved. Heated intraoperative intraperitoneal chemotherapy with mitomycin C was given⁵. After intraoperative therapy, a circular stapled oesophagojejunal anastomosis was performed (ILS 29; Ethicon, Cincinnati, Ohio, USA). The duodenum, which was stapled off as part of the gastrectomy, was oversewn with interrupted sutures. The proximal jejunum was brought out through the left upper quadrant through a generous tunnel. The stoma was constructed as an end-jejunostomy. The Roux-en-Y anastomosis of the first portion of the jejunum to the proximal jejunal segment was not performed. All bile and pancreatic secretions exited via the diverting jejunostomy (*Fig. 1*). If the tumour was thought to show an aggressive character (mucinous carcinoma or hybrid mucinous tumour), 5 days of early postoperative intraperitoneal 5-fluorouracil (5-FU) was administered⁵. Thirty-six patients had perioperative 5-FU.

Patients were maintained on parenteral nutrition for 1–9 months until second-look laparotomy was performed. At this time, all adhesions were taken down, an additional cycle of heated intraoperative intraperitoneal chemotherapy was given and the jejunostomy was closed. If tumour nodules were present, they were cytoreduced before the chemotherapy. If the malignancy retained an aggressive character another 5 days of early postoperative intraperitoneal 5-FU was administered.

All of these patients were included in a prospective morbidity and mortality database. This database was specifically defined to itemize all postoperative events

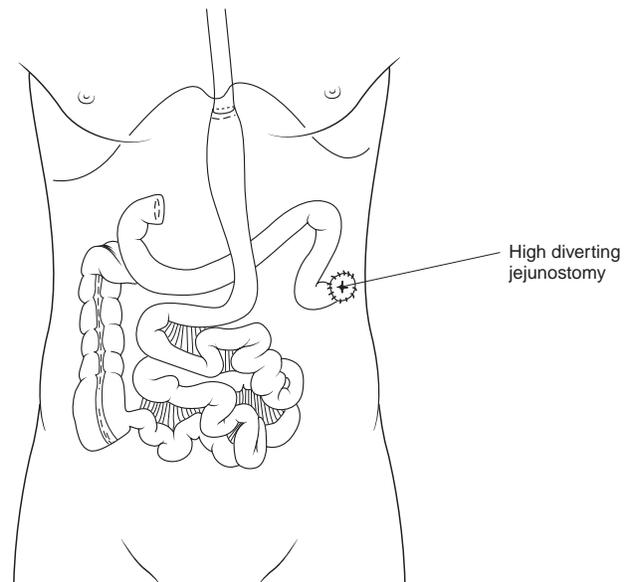


Fig. 1 Gastrectomy with temporary diverting jejunostomy as part of cytoreductive surgery for pseudomyxoma peritonei

while the patient was in hospital. Grade 3 complications were defined as those requiring an invasive intervention, usually an interventional radiology procedure. Grade 4 complications required a return to the operating room.

Results

The median age of the 45 patients was 47 (range 33–66) years. Pathology reported from the definitive cytoreduction was adenomucinosis in 19 patients, hybrid mucinous tumour in 21 and mucinous carcinoma in five. Fourteen patients had no, or only minor surgical procedures before the definitive cytoreduction, but eight had undergone two or three previous attempts at complete cytoreduction at other institutions. Six patients had intestinal obstruction and were maintained at least in part by intravenous feeding before surgery; two of these patients had had multiple previous attempts at cytoreduction at another hospital. In all patients computed tomography (CT) performed just before the cytoreduction showed extensive tumour within the subpyloric space¹⁵. This CT prediction of the need for gastrectomy facilitated a proper consent for surgery before the operation (*Fig. 2*). Forty of the patients had a Karnofsky nutrition score of 1; however, five patients whose disease had progressed to cause intestinal obstruction were showing increasing debilitation from pain and inadequate nutrition. The median interval from diagnosis of pseudomyxoma peritonei to definitive cytoreduction was 23 (range 0–140) months.

Surgical results

In all patients five visceral and parietal peritonectomy procedures were performed before the gastrectomy. In four patients cytoreduction was done without gastrectomy, but gastrectomy was needed at a second operative procedure. In all 45 patients the total gastrectomy was accompanied by a diverting jejunostomy. In 18 patients a total abdominal colectomy was performed along with the total gastrectomy; five also had proctectomy. When both gastrectomy and abdominal colectomy were required this resulted in the construction of both a permanent right-sided end-ileostomy and a temporary left-sided jejunostomy. In six patients the small bowel could be preserved to within a few centimetres of the ileocaecal valve, allowing an ileorectal anastomosis to be performed. The cytoreduction, heated intraoperative chemotherapy and reconstruction took a mean time of 13 (range 9–17) h. Mean blood requirement was 3.0 (range 0–10) units of packed red cells and that for fresh frozen plasma was 9.9 (range 0–16) units. Thirty-eight patients required parenteral nutrition between gastrectomy and jejunostomy closure, despite the use of oral replacement of pancreatic enzymes. The median

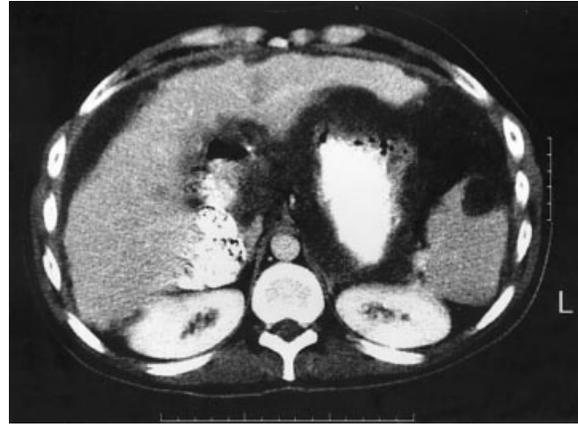


Fig. 2 Computed tomography of the upper abdomen in a patient with mucinous adenocarcinoma from a perforated appendix with advanced pseudomyxoma peritonei. The stomach is encased by mucinous tumour so that the left gastric artery is surrounded, and the tumour is impacted into the omental bursa

interval between cytoreduction and the second-look operation with stoma closure was 5 (range 2–8) months.

Outcome

There was a single postoperative death associated with pancreatitis and an oesophagojejunal anastomotic leak. A second death from other causes occurred 1-year after ostomy closure. A second oesophagojejunal anastomotic leak was associated with intractable postoperative vomiting. There were four reoperations for ileocolic or ileorectal anastomotic leakage, one reoperation for extensive fluid collection without fistula or sepsis, and two reoperations for bleeding. One small bowel fistula and one duodenal fistula were treated without reoperation. Three patients developed a pancreatic fistula. In 11 of the 45 patients there was a grade 3 or 4 complication. The median hospital stay was 37 (range 14–103) days.

Twenty-one of 39 patients who had a second-look laparotomy had visible evidence of persistent and progressive disease; in all but four, all tumour was cleared at the time of second-look surgery. As part of the comprehensive treatment strategy, all but two patients had a second cycle of heated intraoperative intraperitoneal chemotherapy with the combined second-look operation and stoma closure.

Forty-two of these 45 patients are alive and 37 are currently disease free. All patients who were disease free at the completion of second-look surgery have remained free from clinical evidence of recurrence. The median follow-up was 26 (range 0–56) months. All patients have CT of the chest, abdomen and pelvis every 6 months to monitor disease progression or recurrence.

Four significant complications (no deaths) occurred with the second-look operation. One patient developed a fistula at the lower aspect of the closure of the proximal jejunum, probably as a result of improper nasojejunal tube placement. A second patient developed a duodenal fistula after extensive repeat cytoreduction. A third patient developed a bladder fistula and an ileorectal anastomotic leak. A fourth patient developed an abdominal wall fasciitis that required wide debridement and skin grafting. In all four of these patients extensive disease progression was observed at the time of second-look surgery and repeat cytoreduction was attempted.

The high diverting jejunostomy produced a daily mean loss of 650 ml of bile and pancreatic juice, and caused a severe malabsorption despite pancreatic enzyme replacement. These potential problems in management caused little or no difficulty if patients remained on parenteral feeding while the high diverting jejunostomy was functional.

Three-quarters of the patients no longer required parenteral feeding soon after the stoma closure/second-look procedure. All but two patients were free from intravenous feeding within 4 months of the jejunostomy closure. Refeeding of bile was not used in any patient. Intestinal motility continued as normal despite the high diversion so that patients were able to consume a postgastrectomy diet. No adverse events from bacterial overgrowth or intestinal dysmotility occurred.

Discussion

Previous publications on pseudomyxoma peritonei syndrome demonstrated that completeness of cytoreduction was the dominant prognostic feature in this group of patients. The extent of disease before surgery was not important in predicting outcome. Histological grade was significant, but complete clearing of the mucinous tumour was the dominant variable³. The clarity of these data regarding the absolute requirement for completeness of cytoreduction and the predictable disease progression if residual disease was left on the stomach provided the rationale to extend the visceral peritonectomy to include the entire stomach¹⁶. This has improved the ability to achieve a complete cytoreduction in a larger proportion of patients.

The cost-benefit analysis of this treatment plan could be questioned. However, the median age in this group of patients was 47 years. They have many years ahead if they can be cured. From a healthcare perspective it is less expensive to treat these patients definitively and send them back to a productive status in society than to perform repeated debulkings. This argument was developed in a

comprehensive review article on the pseudomyxoma peritonei syndrome³. Nineteen of these 45 patients had a minimally aggressive mucinous appendiceal malignancy resulting in an indolent disease process; additional patients with disease progression may be seen. Five patients known to have persistent disease are currently alive with minimal symptoms. Although pseudomyxoma peritonei is a lethal disease it can be indolent, and survival over several years with a slowly progressive disease does occur.

The magnitude of the commitment these treatments require for the physician, patient and patient's family must not be overlooked. Not only did these patients undergo gastrectomy, but 18 also required a total colectomy to clear all visible evidence of the appendiceal mucinous tumour. They were maintained on parenteral feeding both in hospital and at home during the interval between cytoreduction and stoma closure. A second major operation was required for closure of the diverting jejunostomy and a second look. In nearly all patients one or more family members were present and living in the hospital room with the patients during their in-hospital care. The protracted hospitalization and complex postoperative care required a cancer centre with a commitment to the total care of patients with this rare disease.

In a majority of these patients a complete parietal peritonectomy was required to clear the mucinous tumour. This extensive surgery resulted in a prolonged paralytic ileus and a need for efficient removal of enteric secretions. In the author's experience nasojejunal tubes stenting the oesophagojejunal anastomosis are inadequate for this decompression. The temporary duodenal diversion has provided reliable control of enteric secretions and made cytoreduction with gastrectomy a treatment option for patients with advanced pseudomyxoma peritonei syndrome.

All patients will require a second operation for closure of the high diverting jejunostomy. This allows a second-look procedure for cytoreduction of small amounts of residual mucinous tumour and a second cycle of heated intraoperative and early postoperative intraperitoneal chemotherapy. Second-look surgery may be an essential part of a successful treatment strategy. In a majority of patients a small amount of persistent and progressive mucinous tumour was discovered and treated, despite a completely normal CT scan of the chest, abdomen and pelvis¹⁷. However, four patients had large-volume recurrence of mucinous tumour observed at the time of second look. All four of these patients developed major complications as a result of this renewed aggressive approach to treatment failure with the initial cytoreduction. Repeat cytoreduction of a large volume of disease may not be appropriate from this experience.

Surprisingly few adhesions were encountered at the second-look stoma closure. The thorough intraoperative washing with mitomycin C, immediate postoperative lavage with peritoneal dialysis solution and 5 days of 5-FU lavage resulted in minimal adhesions. Pelvic adhesions remained a problem and required extensive lysis; occasionally adhesions in the extreme left upper quadrant were also problematic. The right subphrenic space and right subhepatic space were not re-explored because of dense adhesions between the surface of the liver stripped of its capsule and the undersurface of the right hemidiaphragm stripped of its peritoneum. Also, the area in and around the oesophagojejunal anastomosis was deliberately avoided.

Second-look surgery is beneficial if the repeat resection is complete¹⁸. However, if additional cytoreductions of mucinous appendiceal tumour are necessary, the beneficial effects are rapidly lost. Requirement for third, fourth and fifth cytoreductions indicates a more aggressive disease process that cannot be eradicated by combined cytoreductive surgery and perioperative intraperitoneal chemotherapy (F. Mohamed and P. H. Sugarbaker, unpublished data).

After the immediate postoperative recovery, two problems remain with this new approach of extensive peritonectomy with total gastrectomy. First, the left upper quadrant stoma remains for approximately 6 months. Proximity of the stoma to the left costal margin, lack of a mound of skin, and a small width of flat skin surface at the edges of the stoma caused initial difficulties in maintaining a watertight appliance. Also, the stoma output is liquid and rich in enzymes, so that even small leaks are troublesome. Some patients requested stoma closure within 6 months because of difficulties with management.

Second, patients must be kept on parenteral nutrition in order to maintain a high level of physical activity before second-look surgery. Although oral food intake was normal, resorption without bile and normal pancreatic enzymes was poor. All but two patients had parenteral feeding discontinued after jejunostomy closure.

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