

ORIGINAL ARTICLE

Digestive fistulas after cytoreductive surgery & HIPEC in peritoneal carcinomatosis

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Summary

Purpose: The development of digestive fistulas is a complication of gastrointestinal operations during cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). In this article we present the incidence, management and outcome of enterocutaneous digestive fistulas after CRS and HIPEC.

Methods: Over the past 10 years (2005-2014), 184 patients with peritoneal carcinomatosis underwent CRS and HIPEC. HIPEC was administered in the operating room immediately after CRS, but in 48 (26%) patients this happened before the formation of intestinal anastomosis or repair of seromuscular tears, using the open (coliseum) technique; in the remaining 137 (74%) patients the anastomoses were performed before HIPEC. All patients were operated on by

the same surgical team.

Results: Of the 185 patients 16 (8.6%) developed an enterocutaneous digestive fistula. Spontaneous fistula closure was observed in 14 (87.5%) patients. The median duration of spontaneous closure was 18 days (range 9-56). Reoperation was needed in 2 (12.5%) patients. There were 2 (12.5%) deaths.

Conclusion: CRS and HIPEC is a well-known treatment modality for peritoneal carcinomatosis. The incidence of digestive fistulas is increased a little compared to that of conventional digestive surgery.

Key words: cytoreductive surgery, enterocutaneous fistula, HIPEC

Introduction

Carcinomatosis has always been considered, in the past and often today, a terminal condition and it was only managed with palliative treatment. Peritoneal carcinomatosis, a frequent evolution of advanced gastrointestinal cancers, represents one of the main indications for hyperthermic treatment following meticulous cytoreductive surgery [1-3].

As surgical technology has improved and chemotherapeutic agents administered have become safer, the complications associated with this treatment approach have decreased [4-6]. Today the mortality and morbidity of cytoreductive surgery (CRS) and HIPEC are similar to those of other major gastrointestinal operations [7]. The most important factor of the decreased number of

complications is the learning curve of the procedure [8,9].

The prevalent complication in most series is digestive fistulas, either in the form of anastomotic leak or bowel perforation away from anastomotic lines. Fistulas have been reported to occur in 3.9 to 34% of the patients [10-12]. Such figures are somewhat higher than the 5% reported for common elective surgery [13].

The aim of our study was to retrospectively evaluate the incidence of gastrointestinal fistulas after CRS and HIPEC.

Methods

Over the past 10 years (2005-2014), 185 patients

with peritoneal carcinomatosis underwent CRS & HIPEC. The goal of surgery in these patients was to visibly clear the abdomen and pelvis of cancer nodules. This required a series of peritonectomy procedures and visceral resections. Normal peritoneum or normal visceral structures were not resected.

All patients received HIPEC in the operating room immediately after CRS, but in 48 patients (26%) this happened before the formation of intestinal anastomoses or repair of seromuscular tears, using the open (coliseum) technique and in the remaining 137 patients (74%) the anastomoses were performed before HIPEC. All patients were operated on by the same surgical team.

The study endpoints were the incidence of digestive enterocutaneous fistulas and the management and outcome of this complication in CRS & HIPEC patients.

Results

Of 185 patients treated with CRS & HIPEC for peritoneal carcinomatosis 16 (8.6%) developed an enterocutaneous digestive fistula.

The origins of the fistulas are presented in Table 1.

The origin of peritoneal carcinomatosis in these 16 patients (6 men and 10 women) was: pseudomyxoma peritonei in 2, ovarian cancer in 8, gastric cancer in 1, colon cancer in 3, mesothelioma peritonei in 1 and appendiceal carcinoma in 1. Patient median age was 62 years (range 44-72).

All patients had received preoperative chemotherapy and 6 of them (37.5%) were preoperatively malnourished. In all patients peritoneal disease was very extensive, as reflected by the median Peritoneal Cancer Index (PCI) of 24 (range 12-32).

The type of surgery in these patients is depicted in Table 2.

Spontaneous closure of the fistula was observed in 14 patients (87.5%). The median duration for spontaneous closure was 18 days (range 9-56). Reoperation was needed in 2 patients (12.5%), one on a patient with a small bowel fistula with a high output after the fourth week and one on a patient with a colon fistula due to intra-abdominal sepsis.

There were 2 deaths (12.5%), one of the re-

Table 2. Type of surgery and HIPEC in 16 patients with digestive fistulas

Type of surgery	N	%
Splenectomy	2	12.5
Cholecystectomy	16	100
Omentectomy	16	100
Hysterectomy	8	50.0
Gastrectomy	2	12.5
Complete colectomy	6	37.5
Douglas resection	8	50.0
Small bowel resection	12	75.0
Partial colectomy	4	25.0
Drugs used in HIPEC (60min)		N
Mitomycin	3	
Oxaliplatin	8	
Oxaliplatin + doxorubicin	5	

Table 3. Final outcome of fistulas

Spontaneous closure: 14/16 (87.5%)
Time to fistula closure, either spontaneous or surgical: 16.4 days (range 7-52)
Treatment for spontaneous closure
TPN + octreotide analogue sc: 11/16 (68.7%)
EN + octreotide analogue sc: 3/16 (18.7%)
TPN + EN + octreotide analogue sc: 2/16 (12.5%)
Reoperation: 2/16 (12.5%)
Mortality: 2/16 (12.5%)
One patient after reoperation due to ARDS & sepsis
One patient due to candida sepsis

TPN: total parenteral nutrition, EN: enteral nutrition, sc: subcutaneous, ARDS:acute respiratory distress syndrome

operated patient with the small bowel fistula due to acute respiratory distress syndrome (ARDS) because of pneumonia from candida and a second death of a patient with a small bowel fistula due to sepsis.

Fistula outcomes are presented in Table 3.

Discussion

Digestive fistulas are first treated with three main steps: resuscitation, control of sepsis and nutritional support. The main tools are total parenteral nutrition, hydration, antibiotics and somatostatin analogues in order to control the fistula output [14,15]. The final step, if necessary, is definitive surgery to restore gastrointestinal tract continuity.

In a systematic review by Chua et al. [7] of

Table 1. Digestive fistulas (N=16/8.6%) after cytoreductive surgery & HIPEC in 185 patients

Fistula location	N	%
Small bowel	5	31.5
Pancreas	3	18.7
Gallbladder	3	18.7
Colon	3	18.7
Oesophagus	2	12.5
Total	16	100

studies with patients subjected to SCR and HIPEC, published before August 2008, it was concluded that the morbidity and mortality of CRS & HIPEC were similar to those of other major gastrointestinal operations [7].

The potential advantages of using HIPEC compared to standard systemic chemotherapy include increased exposure of the peritoneal surface to antineoplastic drugs, increase of drug penetration into the tissues, a synergistic effect of hyperthermia and an independent cytotoxic effect of hyperthermia [16].

Are there any complications related to hyperthermia and simultaneous drug administration?

It is clear that the effects of this combined regional treatment are not limited to the peritoneal cavity, and the deep effect that these treatments have on wound healing is shown by the increased incidence of gastrointestinal complications.

The incidence of gastrointestinal fistulas after conservative cancer surgery was reported to be 5% while after CRS & HIPEC it increased to 8% [14]. In our study it was 8.6% and the presence of digestive fistula was significantly associated with the operative time, the number of anastomoses, previous systemic chemotherapy or radiotherapy and the nutritional status. These are also important factors concerning the spontaneous closure of fistulas [17,18].

Kusamura et al. in a study of 205 patients treated with CRS & HIPEC reported that the rate of fistulas was 11% [19]. They found that the extent of cytoreduction and a dose of CDDP ≥ 240 mg were independent risk factors for digestive fistulas.

Youssef et al. conducted a study of 456 pa-

tients with pseudomyxoma peritonei syndrome of appendiceal origin and found an incidence of digestive fistulas of 4.4%. Analysis of risk factors was not provided [20].

The somatostatin analogue octreotide can significantly decrease fistula output and while routine use remains controversial, findings suggest a reduced time to fistula closure and scant evidence exists of increased probability of spontaneous closure [17].

Total parenteral nutrition provides initial nutritional support, while control of infection and maturation of the fistula tract occur. Normal intestinal function and motility usually return once abdominal sepsis is controlled and fluid and electrolyte imbalances are corrected. Enteral feeding may also be initiated. In our cases, this was applied twice in patients with oesophageal fistulas after total gastrectomy procedures, via a catheter placed distally to the fistula. We started with an elementary diet while the fistula output was monitored [21].

In conclusion, CRS & HIPEC is a well known treatment modality for peritoneal carcinomatosis. The morbidity of this procedure is related to aggressive surgical procedure, hyperthermia and locoregional chemotherapy. The incidence of digestive fistulas is a little superior to that of conventional digestive surgery. The data from different studies suggest that CRS & HIPEC is a reasonably safe treatment for selected patients with peritoneal carcinomatosis in centers of excellence with acceptable digestive morbidity, compared to that of Whipple's procedure, D2 gastrectomy, or multivisceral resections [22].

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