

ORIGINAL ARTICLE

Short bowel syndrome after cytoreductive surgery and HIPEC: nutritional considerations

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Summary

Purpose: The aim of this study was to present a group of patients with <150 cm of small intestine after cytoreductive surgery (CRS)+hyperthermic intraperitoneal chemotherapy (HIPEC) and the special problems arising from this condition.

Methods: From November 2005 to November 2013, 130 patients were treated for peritoneal carcinomatosis (PC) with CRS+HIPEC. Ten patients (7.7%) were left with a short bowel due to anatomical and surgical reasons. All these patients were subjected to ileostomy. Four patients (40%) were treated for ovarian carcinoma, 4 (40%) for colon and appendiceal carcinoma, 1 for peritoneal mesothelioma and 1 patient for primary peritoneal carcinoma. The completeness of cytoreduction (CC) score was CC-0 in 4 patients (40%), CC-1 in 3 (30%) and CC-2 in 3 (30%).

Results: The mean length of the remaining small bowel was 105 cm (range 80-150). Mean hospitalization was 42 days vs 24 days in other patients with CRS+HIPEC

($p<0.002$). The daily ileostomy output increased between the 3rd to 4th week as a result of oral feeding and decreased at the 4th week due to somatostatin analogue administration and possible intestinal adaptation. The mean ileostomy output at 6 months was 810 ± 100 ml vs 1590 ± 210 ml the first month after CRS+HIPEC ($p<0.001$). The overall morbidity and mortality rate was the same as in patients without extensive resection. The impact of small bowel syndrome (SBS) on overall survival was very important, as the mean overall survival in the SBS group was 28.6 months vs 41 months in other CRS+HIPEC patients ($p<0.001$).

Conclusions: SBS is sometimes inevitable in order to perform optimal cytoreduction. Special management is required for these patients, including special nutritional efforts and home total parenteral nutrition (TPN). Extensive small bowel resection may constitute a contraindication in the management of peritoneal carcinomatosis.

Key words: cytoreductive surgery, HIPEC, short bowel syndrome

Introduction

Prolonged survival of patients with peritoneal carcinomatosis has been reported in patients treated with CRS plus HIPEC.

The most important factor which improves survival in these patients is completeness of cytoreduction, consisting of numerous surgical procedures, depending on the extent of peritoneal disease. It is important to define that CRS means peritonectomy procedures as described by Sugarbaker [1], and not debulking surgery.

Peritonectomy procedures consist of two big surgical components, parietal and visceral, greater omentectomy, splenectomy, cholecystectomy, liver capsule resection, partial gastrectomy, subtotal colectomy and resection of mesentery and stripping of parietal and diaphragmatic peritoneum. These procedures sometimes lead to SBS, which is characterized clinically by severe malabsorption, chronic diarrhea, dehydration and electrolyte abnormalities. The severity and management of SBS depend on the site and extent of the intestinal resection, the presence of the ileocecal

valve, the status of the residual intestine and the degree of intestinal adaptation.

The aim of this study was to retrospectively analyse patients with less than 150 cm of remaining small intestine after CRS+HIPEC and focused on the special nutritional problems which arose from this condition.

Methods

This study was a retrospective analysis of patients with SBC following cytoreductive surgery and HIPEC. From November 2005 to November 2013, 130 patients with PC were treated with CRS and HIPEC by our team.

In 10 patients (7.7%), in the attempt for maximal cytoreduction, major resections had to be performed, including mesentery resection, resulting in SBC. Ileostomy was created in all (100%) patients.

Figure 1 displays the malignancies for which the patients were subjected to CRS and HIPEC. PC was due to ovarian cancer in 4 of our patients (40%), to colonic or appendiceal cancer in another 4 (40%), to peritoneal mesothelioma in 1 (10%) and to primary peritoneal cancer in another 1 patient (10%).

All patients had agreed to be included in this study and have signed informed consent prior to surgery.

Statistics

Patient characteristics and surgical outcome were analyzed by descriptive statistics. Categorical variables were compared using χ^2 test or Fisher's exact test where appropriate. Normally distributed variables were compared using t-test as appropriate and non parametric tests were used when variables were not normally distributed. Survival was measured with the Kaplan-Meier methods and log rank test. A p value <0.05 was considered statistically significant.

All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) v. 17 and Microsoft Office Excel.

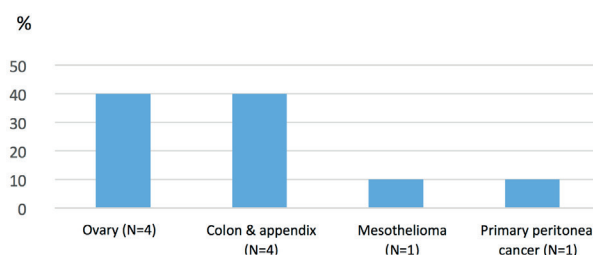


Figure 1. Origin of peritoneal carcinomatosis.

Results

Table 1 displays the disease and operation characteristics and patient survival, and Figure 1 shows the origin of PC. In 7 (70%) of our patients, optimal cytoreduction was achieved (CC scores: CC-0 and CC-1), while in the remaining 3 (30%) patients, a CC-2 score was achieved (Table 1). The mean length of the remaining small intestine was 105 cm (range 80-150).

The mean length of hospital stay was 42 days in patients with SBS, vs 24 days in the rest of our CRS+HIPEC patients ($p < 0.002$). However, no difference was observed in the rates of immediate postoperative morbidity or mortality.

All patients were followed up postoperatively for a median of 30 months (range 12-120). To this day, only 3 (30%) SBS patients are alive (Table 1).

Figure 2 presents the causes of death, the most common being disease progression (30%), followed by sepsis (20%), and dehydration leading to renal failure (20%).

The mean survival was 28.6 months in the short bowel patients, vs 41 months in the rest of CRS+HIPEC patients ($p < 0.01$).

The mean daily ileostomy output was measured up to 6 months postoperatively and is pre-

Table 1. Disease and operation characteristics and patient survival

Patient no.	Tumor location	CC	Remaining small bowel length (cm)	Survival (months)	Status (Alive / dead)
1	ovary	1	150	18	D
2	ovary	0	110	72	A
3	colon	1	120	44	D
4	colon	0	90	60	A
5	ovary	0	100	56	A
6	mesothelioma	2	90	14	D
7	appendix	2	80	3	D
8	ovary	1	110	8	D
9	peritoneum	0	100	6	D
10	appendix	2	100	5	D

CC: completeness of cytoreduction, D: dead, A: alive

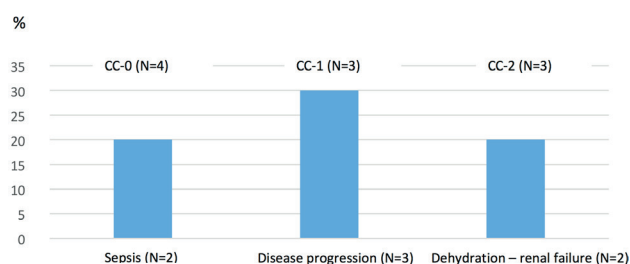


Figure 2. Causes of death.

sented in Table 2. The output at 6 months was 810 ± 100 ml vs 1590 ± 210 ml the first month after CRS+HIPEC ($p < 0.01$). An increase in the output was observed over the first postoperative month, following the introduction of oral feeding, which was reduced later on, after the administration of a somatostatin analogue at 2 months.

Two months postoperatively, all patients had to be supported with the administration of home TPN. Two patients needed to receive TPN once weekly (20%), 4 received TPN twice weekly (40%) and another 4 patients received TPN three times a week (40%) (Table 3).

Discussion

This is the first study reporting the outcomes of SBS in patients undergoing CRS and HIPEC due to PC.

CRS ought not to be confused with debulking surgery, which aims at the removal of all macroscopic intraperitoneal disease. CRS, as it has been described by Sugarbaker [1,2], consists of a series of peritonectomy procedures and visceral resections aiming at the complete removal of tumor from the abdominal cavity, with the goal of optimal cytoreduction i.e. residual tumor less than 0.25 cm in diameter.

HIPEC is indicated after CRS for PC of several origins, such as ovarian, colorectal, gastric and pancreatic cancers, peritoneal mesothelioma and pseudomyxoma peritonei [3].

At the expense of achieving optimal cytoreduction, major splanchnic resections are often inevitable, including not only rectosigmoid colon resections, but also small intestine resections, due to the presence of tumor implants.

The SBS occurs when the total length of the small intestine is insufficient to support adequate nutrient and fluid absorption. Seventy five percent of cases of SBS occur from a massive intestinal resection (such as the ones performed during CRS, as described above), while 25% result from multiple sequential resections [4,5].

Table 2. Ileostomy output (ml) / 24 hrs

Patient no.	1st week	2nd week	4th week*	2 months**	3 months	6 months
1	800	1100	1000	800	600	650
2	900	1400	1200	1000	1100	900
3	800	900	1000	900	1000	700
4	1100	1600	2500	700	700	600
5	1000	1200	1400	1100	800	700
6	1300	1500	1200	2000	1800	1500
7	1500	1300	3000	2000	1800	
8	900	1100	1200	1400	1100	800
9	800	900	1600	1100	900	700
10	950	1600	1800	1450		

* oral meal (1500 kCal), ** somatostatin analogue

Table 3. Total parenteral nutrition (TPN) after 2 months

Patient no.	TPN / week no.
1	1
2	2
3	2
4	3
5	3
6	2
7	3
8	1
9	2
10	3

Once a week 20%, 2 per week 40%, 3 per week 40%. Once + 2 per week = good quality of life; 3 per week = intermediate quality of life

The clinical manifestations of SBS include diarrhea, fluid and electrolyte deficiency and malnutrition. Whether the patient will permanently depend on parenteral nutrition is influenced by the site and extent of the intestinal resection, the presence of the ileocecal valve, the status of the residual bowel and the degree of intestinal adaptation.

There are three phases of the SBS: the post-operative hypersecretion phase, the adaptation phase and the maintenance/stabilization phase [6].

During the first phase, fast gastric emptying and fluid passage through the bowel inhibit the proper absorption of nutrients. Moreover, gastric hypersecretion and disruption of the enterohepatic circulation greatly contribute to diarrhea, often resulting in excessive fluid loss. Therefore, it is of utmost importance to monitor closely the daily input/output balance in order to prevent severe dehydration and to maintain energy balance and steady body weight. While oral feeding

is advised to begin as early as possible, the stoma output reaches its maximum after food and drink consumption. In our study, this maximum output was observed at the first postoperative month, after the full introduction of oral feeding. Most patients with a short bowel require parenteral nutrition for 7-10 days postresection and postoperative hydration is mainly achieved with normal saline administration. Medical management in this early phase includes the administration of H₂-receptor antagonists or proton pump inhibitors, cholestyramine and octreotide, in the attempt to reduce diarrhea/steatorrhea.

Over the second phase, the phenomenon of intestinal adaptation (adaptive hyperplasia) is observed, characterized by significant morphological and functional changes. The remaining intestine changes macroscopically with dilatation, thickening and an increase in length [7], in the attempt to restore absorption of macronutrients, macrominerals and water to that prior to the resection [8]. Cellular hyperplasia, villous hypertrophy and alteration of motility also occur [9]. These changes are increased with more extensive resections, appear more prominently in the ileum [10] and result in an improved absorptive capacity [11]. Sufficient energy intake is achieved initially with a high-carbohydrate, high-protein diet. Besides maintaining an adequate energy intake (also with the aid of parenteral nutrition), attention should be paid on the mineral balance, especially sodium, potassium and magnesium. Administration of growth hormone or glucagon-like peptide 2 (GLP-2) has shown to improve intestinal absorption in parenteral nutrition-dependent patients [12,13].

As the bowel adapts (stabilization phase), weaning from parenteral nutrition may become feasible. The length of the small bowel, the presence of colon, the time on parenteral nutrition (>2 years) and the amount of energy the patient can derive from enteral feeding are the factors predicting whether intestinal failure is permanent [11]. Since parenteral nutrition has been associated with increased morbidity and mortality (central venous catheter infections, liver disease) and reduced quality of life [12,14], attempts should be made to reduce or even stop its administration.

In this study, all our patients had to be supported by home parenteral nutrition 2 months after surgery, reporting a good quality of life (those receiving 1 or 2 doses weekly; 60%) or an intermediate quality of life (those receiving parenteral nutrition 3 times a week; 40%). Intestinal adaptation and stabilization are also eminent in the results of our study, as we have observed that the ileostomy output was significantly lower 6 months after surgery compared to the output over the first postoperative month.

Conclusion

Extensive resections during CRS for PC sometimes result in SBS. The management of this syndrome presents a challenge for both the surgeon and the nutritionist and requires a multimodality approach. The increased morbidity and mortality arising from this condition should be taken into consideration and the necessity of extensive small bowel resections may be re-evaluated in the management of PC.

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