

Intraperitoneal Chemohyperthermia Using a Closed Abdominal Procedure and Cytoreductive Surgery for the Treatment of Peritoneal Carcinomatosis: Morbidity and Mortality Analysis of 216 Consecutive Procedures

O. Glehen, MD, D. Osinsky, MD, E. Cotte, MD, F. Kwiatkowski, MS, G. Freyer, MD, PhD, S. Isaac, MD, V. Trillet-Lenoir, MD, PhD, A. C. Sayag-Beaujard, MD, Y. François, MD, J. Vignal, MD, and F. N. Gilly, MD, PhD

Background: Peritoneal carcinomatosis has been regarded as a lethal clinical entity. Recently, aggressive treatments combining intraperitoneal chemohyperthermia (IPCH) with cytoreductive surgery have resulted in long-term survival in selected patients. The aim of this trial was to analyze the mortality and morbidity of 216 consecutive treatments of peritoneal carcinomatosis by IPCH by using a closed abdominal procedure combined with cytoreductive surgery.

Methods: Between February 1989 and August 2001, 207 patients who underwent 216 IPCH procedures using a closed abdominal procedure with mitomycin C, cisplatin, or both were prospectively studied.

Results: The postoperative mortality and morbidity rates were 3.2% and 24.5%, respectively. The most frequent complications were digestive fistula (6.5%) and hematological toxicity (4.6%). Morbidity was statistically linked with the carcinomatosis stage ($P = .016$), the duration of surgery ($P = .005$), and the number of resections and peritonectomy procedures ($P = .042$). Duration of surgery and carcinomatosis stage were the most common predictors of morbidity.

Conclusions: The frequency of complications after IPCH and cytoreductive surgery was mainly associated with the carcinomatosis stage and the extent of the surgical procedure. The IPCH closed abdominal procedure has shown an acceptable frequency of adverse events.

Key Words: Morbidity—Mortality—Cytoreductive surgery—Hyperthermia—Intraperitoneal chemotherapy.

Peritoneal carcinomatosis is a common evolution of cancer of the gastrointestinal tract (48% of gastric cancers with serosal erosion¹) and is the terminal stage of

disease, because most patients with carcinomatosis die within 6 months.² Malignancies that present within the abdominopelvic cavity often cause their great morbidity and mortality through progressive involvement of the peritoneal surfaces. During the last decade, there has been a renewed interest in peritoneal surface malignancy. New aggressive therapeutic approaches have been proposed and are currently under evaluation. Treatments that prevent or eradicate cancer at the resection site and on peritoneal surfaces may contribute to improvements in survival. After an experimental study in dogs,³ intraperitoneal chemohyperthermia (IPCH) has been used for the treatment of peritoneal carcinomatosis from gynecological and nongynecological malignancies since 1989.⁴ In 1995, peritonectomy was first described as a new

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From the Departments of Surgery (OG, DO, EC, YF, JV, FNG), Oncology (GF, VT-L), Anaesthesiology (ACS-B), and Pathology (SI), Centre Hospitalier Lyon-Sud, Pierre Bénite Cédex, France; Oncologic Hyperthermia Laboratory-Equipe Accueil "Ciblage Thérapeutique en Oncologie" (OG, FNG), Université Claude Bernard Lyon-1, Oullins, France; and Bio-Statistical Unit (FK), Centre Jean Perrin, Clermont-Ferrand, France.

Address correspondence and reprint requests to: François Noël Gilly, MD, PhD, Surgical Department, Centre Hospitalo-Universitaire Lyon Sud, 69495, Pierre Bénite Cedex, France; Fax: 33-478-863-343; E-mail: francogi@lyon-sud.univ-lyon1.fr.

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surgical approach for carcinomatosis.⁵ It is as an aggressive procedure with high postoperative morbidity rates,⁶ but it is able to downstage carcinomatosis and improve long-term survival for selected patients.^{7,8} In 1998, we decided to combine peritonectomy procedures with IPCH for patients with peritoneal carcinomatosis from gastrointestinal and gynecological malignancy.^{9,10} The morbidity and mortality analysis of IPCH treatment alone or combined with peritonectomy procedures is presented here.

PATIENTS AND METHODS

IPCH was first used for the treatment of carcinomatosis at the surgical department of Lyon-Sud Hospital Center in February 1989. One hundred sixty patients were enrolled in a phase II clinical trial between 1989 and 1997.^{4,11} Informed consent was obtained from all patients before surgery. Patients underwent IPCH without extensive cytoreductive surgery. IPCH was performed with mitomycin C (MMC) for carcinomatosis of gastrointestinal origin, with cisplatin (CDDP) for carcinomatosis of ovarian origin, and with both drugs for mesothelioma, pseudomyxoma peritonei, or carcinomatosis from carcinoma of unknown origin. The technique^{3,12} and the pharmacokinetic studies^{13,14} of our closed abdominal technique have been reported. After this initial phase II study, in light of the interesting survival results published by Sugarbaker,⁵ we conducted a second phase II study from 1998 to 2001. Fifty-six patients with peritoneal carcinomatosis were treated with IPCH combined with cytoreductive surgery and peritonectomy procedures.^{9,10} Nine patients were involved in both trials. The data presented here combine these phase II studies and were prospectively recorded between February 1989 and August 2001 for 216 IPCH treatments in 207 patients with peritoneal carcinomatosis from gynecological and nongynecological origin.

Surgical Procedure

Under general anesthesia and with hemodynamic monitoring, abdominal exploration was performed through a midline laparotomy (from xiphoid to pubis). Surgical resection of the primary tumor was performed whenever possible according to surgical oncological principles (lymphadenectomy and acceptable margins). Once the primary tumor was removed, peritonectomies were performed; these were adapted to the location of the peritoneal malignant nodules as guided by the surgeon's exploration and frozen-section biopsy samples. Peritonectomies were performed only for peritoneal surfaces involved by tumor. These peritonectomy procedures

were performed according to Sugarbaker's⁵ surgical guidelines. Locations of peritonectomies performed were recorded before surgery on a specific form: (1) right diaphragmatic cupola, (2) left diaphragmatic cupola, (3) greater omentum, (4) lesser omentum, (5) omental bursa, (6) right colon gutter, (7) left colon gutter, (8) Douglas' pouch, (9) anterior wall peritoneum, (10) posterior wall peritoneum, (11) Glisson capsula, and (12) mesenteric peritoneum.

The assessment of the completeness of cytoreduction (CCR) by cytoreductive surgery performed by the surgeon at the end of the procedure was classified into three categories. A CCR-0 indicated that no macroscopic residual cancer remained. CCR-1 indicated that the diameter of every residual nodule was <5 mm. CCR-2 indicated that the diameter of every residual nodule was >5 mm.

IPCH Device

At the end of each surgical procedure, an IPCH infusion was performed under general anesthesia and general hypothermia (32°C induced throughout the peritonectomy procedure by cold wraps on both lower extremities and an ice hat). Before closure of the laparotomy, two inflow drains were inserted under the left and right diaphragmatic cupola (30F silicone drain; Bard Cardio-pulmonary Division, USA), and a third drain (outflow) was inserted in the pouch of Douglas (32F). Temperature probes (thermic probes; Mallinckrodt SA and Cair SA, Lozanne, France) were also inserted within the abdominal cavity (behind the liver pedicle and near the first jejunal loop). Other temperature probes were set up outside the abdominal cavity on the inflow and outflow drains (8 cm from the skin) and inside the bladder within a Foley catheter. The laparotomy incision was then closed, and the inflow and outflow drains were connected to a closed sterile circuit in which a 4- to 6-L perfusate (Travenol Laboratory, Norfolk, England) was circulated by means of an electromagnetic pump at a flow rate of 500 mL/minute. The closed sterile circuit was heated by means of a thermal exchanger (Dideco, France) connected to a heating circuit. Intra- and extra-abdominal temperature probes were connected to a digital thermometer (Cair SA) and monitored every 10 minutes (Fig. 1). IPCH was performed for 90 minutes with careful monitoring of respiratory and hemodynamic parameters at inflow temperatures ranging from 46°C to 48°C.

Type of Intraperitoneal Chemotherapy

For peritoneal carcinomatosis from gastrointestinal origin, MMC was used at the dose of .7 mg/kg (maximum dose of 60 mg). For peritoneal carcinomatosis from

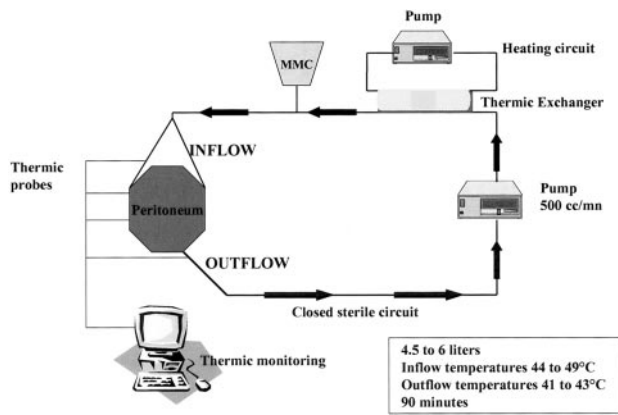


FIG. 1. Intraperitoneal chemohyperthermia device.

ovarian origin, CDDP was used at a dose of 1 mg/kg (maximum dose of 80 mg). For peritoneal carcinomatosis from peritoneal malignant mesothelioma, from pseudomyxoma peritonei, and of unknown origin, .5 mg/kg of MMC and .7 mg/kg of CDDP were combined intraperitoneally. MMC, CDDP, or both were added to the peritoneal dialysis liquid at the beginning of IPCH.

Samples of blood, urine, and perfusate were collected during IPCH at 45 and 90 minutes, and MMC and CDDP concentrations were measured by high-performance liquid chromatography.¹³ MMC concentrations were measured at 24 hours and CDDP concentrations were measured at 12, 24, and 72 hours after IPCH in blood, urine, and abdominal drainage.

Patients

Two hundred sixteen IPCH procedures were performed in 207 patients with peritoneal carcinomatosis (Table 1). There were 78 men (38%) and 129 women (62%), with a mean age of 51.6 years (SD, 11.4 years; range, 20–73 years). Primary tumors were ovarian cancer (n = 67), colorectal cancer (n = 60), gastric cancer (n = 51), pseudomyxoma peritonei (n = 12), peritoneal malignant mesothelioma (n = 10), biliopancreatic malignancies (n = 6), small-bowel cancer (n = 6), unknown primary origin (n = 2), hepatocellular cancer (n = 1), and tumor of the urachus (n = 1). Carcinomatosis stages (Table 2) were 1 or 2 in 92 cases and were 3 or 4 in 124 cases before treatment. Forty-seven patients had large-volume malignant ascites at the time of treatment.

Of 216 procedures, 108 involved IPCH given 8 to 30 days after surgical resection of the primary tumor. These patients underwent surgery at a different hospital and were referred after surgery to our center for cytoreductive surgery, IPCH treatments, or both. The remaining

TABLE 1. Patient characteristics

Variable	Data
No. of patients	207
No. of IPCH and/or cytoreduction procedures	216
No. of patients receiving 2 IPCH and/or cytoreduction procedures	9
No. of patients receiving IPCH and cytoreduction	73
Sex	
Male	78
Female	129
Age (yr)	
Mean	51.6
Range	20–73
Primary tumor	
Ovarian cancer	67
Colorectal cancer	60
Gastric cancer	51
Pseudomyxoma peritonei	12
Peritoneal malignant mesothelioma	10
Biliopancreatic malignancy	6
Small-bowel cancer	6
Unknown primary origin	2
Hepatocellular cancer	1
Tumor of the urachus	1
Carcinomatosis staging	
Stage 0	0
Stage 1	33
Stage 2	59
Stage 3	50
Stage 4	74
Completeness of cytoreduction (CCR)	
CCR-0	37
CCR-1	98
CCR-2	81

IPCH, intraperitoneal chemohyperthermia.

procedures were all performed at our institution: 88 procedures involved IPCH given immediately after the surgical removal of the primary tumor, and 20 procedures involved IPCH performed for metachronous peritoneal carcinomatosis or for peritoneal carcinomatosis recurrence.

In 73 of these 216 procedures, we performed an extensive cytoreductive surgery with peritonectomy procedures immediately before IPCH. All surgical anastomoses were fashioned before the perfusion. Details on digestive organ resections and peritonectomies are listed

TABLE 2. Peritoneal carcinomatosis staging¹²

Stage	Peritoneal carcinomatosis description
0	No macroscopic disease
1	Malignant granulations <5 mm in diameter localized in one part of the abdomen
2	Malignant granulations <5 mm in diameter diffuse to the whole abdomen
3	Localized or diffuse malignant granulations 5 mm to 2 cm in diameter
4	Localized or diffuse large malignant masses (>2 cm in diameter)

in Table 3. The mean number of peritonectomy procedures was 2.4 per patient (SD, 2.9; range, 0–13). The mean number of anastomoses, including bowel anastomoses and pyloroplasty, was .6 (SD, .89; range, 0–4). Repairs of seromuscular tears or tears of the bowel mesentery were not included in the analysis. The mean number of resections was .9 per patient (SD, .7; range, 0–7). At the end of the surgical procedure, 37 patients (17%) were considered a CCR-0, 98 patients (45%) were considered a CCR-1, and 81 patients (38%) were considered a CCR-2. The mean duration of surgery (excluding IPCH) was 3.4 hours (SD, 1.7; range, 1.5–12.5 hours).

Variables

Morbidity variables were organized into 13 categories that were graded 0 to IV by the National Cancer Institute's common toxicity criteria and were as follows: (1) any complication, (2) digestive fistula, (3) hematological toxicity, (4) prolonged ileus after the 14th postoperative day, (5) cardiovascular toxicity, (6) wound sepsis, (7) intraperitoneal abscess, (8) pleuritis, (9) pulmonary complication, (10) pulmonary embolism, (11) renal insufficiency, (12) postoperative bleeding, and (13) systemic sepsis. The main morbidity variables were analyzed for

an association with preoperative variables (sex, age, primary origin, and carcinomatosis stage) and with surgical variables (first or second procedure, CCR, number of anastomoses, number of peritonectomy procedures/resections, and duration of surgery).

Statistical Analysis

Data were collected and analyzed with a commercially available program (Statview 4.5; Abacus Inc., Berkeley, CA) and are expressed as mean, SD, and range. Univariate analysis were performed by using the χ^2 test for categorical variables and by using Student's *t*-test, the Kruskal-Wallis H test, and Spearman rank correlation for continuous data. Logistic regression was used in case of multiple analysis to discriminate among various influences on morbidity.

RESULTS

The mean hospital stay was 11.8 days (SD, 5.5 days; range, 4–31 days). Seven patients (3.2%) died from treatment-related complications (Table 4). All seven patients died before discharge from the hospital.

Of 216 procedures, 51 were followed at least by 1 combined grade III/IV complication (Table 5). Digestive fistulas (6.5%) occurred on average on the 16th postoperative day (range, 2–24 days). One of the 14 fistulas was spontaneous and was not the consequence of an anastomotic leakage. Of the nine cases of prolonged ileus, 7 occurred in the first 5 years of the study. A total of 98 grade III or IV complications were observed after 51 procedures. The average number of major complications among these 51 procedures was 1.9.

In a univariate analysis, carcinomatosis stage, primary origin of the carcinomatosis, duration of surgery, and number of resections and peritonectomy procedures correlated statistically with the occurrence of one complication (Table 6). Duration of surgery and carcinomatosis stage were the most common predictors of morbidity, each with three statistically significant associations. For duration of surgery, there was the occurrence of one complication ($P = .005$), digestive fistula ($P < .001$), and intraperitoneal abscess ($P = .010$). For carcinomatosis stage, there was the occurrence of one complication ($P = .016$), digestive fistula ($P = .002$), and systemic sepsis ($P = .012$).

A multivariate analysis using a logistic regression model was performed to determine which clinical variables were most strongly correlated with the presence of combined grade III/IV morbidity. All clinical variables that were close to significance ($P < .10$) by univariate analysis were included in the model. The carcinomatosis

TABLE 3. Details of cytoreductive surgery: resections and peritonectomy locations

Variable	n
Resections	
Right colectomy	31
Left colectomy	14
Transverse colectomy	5
Subtotal colectomy	2
Gastrectomy	10
Splenectomy	7
Cholecystectomy	15
Liver resection	4
Left pancreatectomy	2
Small-bowel resection	32
Diaphragmatic resection	4
Low anterior resection	3
Right nephrectomy	1
Oophorectomy	22
Total hysterectomy	10
Peritonectomy procedures	
Right diaphragmatic cupola	26
Left diaphragmatic cupola	12
Great omentum	67
Lesser omentum	23
Omental bursa	10
Right colon gutter	48
Left colon gutter	29
Douglas pouch	36
Anterior wall peritoneum	17
Posterior wall peritoneum	10
Glisson's capsule	8
Mesenteric fulguration	57

TABLE 4. Causes of postoperative mortality of 216 treatments combining intraperitoneal chemohyperthermia (IPCH) with or without cytoreductive surgery

Patient No.	Sex	Age (y)	Diagnosis	Treatment	Cause of death	Postoperative/day
1	F	70	Unresectable colon ADK, stage 4 PC	CCR-2 resection, IPCH	Septic shock	5
2	M	49	pT4N2 colon ADK, stage 4 PC	Left colectomy, cholecystectomy, CCR-2 resection, IPCH	Anastomotic fistula, peritonitis	27
3	F	51	Unresectable gastric ADK, stage 3 PC	CCR-2 resection, IPCH	Pulmonary embolism	4
4	F	58	pT4Nx gastric ADK, stage 3 PC	Total gastrectomy, colectomy, CCR-2 resection, IPCH	Anastomotic fistula, multiorgan failure	4
5	F	65	Pseudomyxoma peritonei, stage 3 PC	CCR-2 resection, IPCH	Aplasia	5
6	F	71	Ovarian cancer, stage 3 PC	Total hysterectomy, CCR-1 resection, IPCH	Myocardial necrosis	5
7	F	41	Ovarian cancer, stage 2 PC	CCR-1 resection, IPCH	Acute renal insufficiency	10

PC, peritoneal carcinomatosis; ADK, adenocarcinoma; CCR, completeness of cytoreduction.

stage and the duration of surgery were the two variables that were significantly associated with the presence of major morbidity ($P = .013$ and $P = .002$, respectively).

No grade III/IV hematological toxicity was noticed when MMC was used alone. All grade III/IV hematological toxicities were observed after the use of CDDP alone or in combination with MMC. Among the 10 patients who presented with grade III/IV hematological toxicity, 8 patients had been previously treated by >6 cycles of systemic chemotherapy.

The morbidity rate was 30.5% for patients treated by the combination of cytoreductive surgery with IPCH and was 19.4% for patients treated by IPCH alone ($P = .098$). It was 20% after CCR-0 or CCR-1 resection and 28.3% after CCR-2 resection ($P = .183$). Of the nine patients who underwent a second procedure, one died from a postoperative pulmonary embolism, one presented with an intra-abdominal abscess, and one presented with pleuritis.

TABLE 5. Morbidity of 216 treatments combining intraperitoneal chemohyperthermia with or without cytoreductive surgery

Morbidity	n	%
Digestive fistula	14	6.5
Hematological toxicity	10	4.6
Prolonged ileus	11	5
Wound abscess	9	4.1
Pleuritis	7	3.2
Systemic sepsis	7	3.2
Intraperitoneal abscess	5	2.3
Postoperative bleeding	4	1.8
Line sepsis	4	1.8
Deep vein thrombosis	4	1.8
Renal insufficiency	3	1.3
Respiratory distress	3	1.3
Pulmonary embolism	3	1.3
Myocardial necrosis	1	.4
Neurological complication	1	.4
Combined grade III/IV morbidity	51	24.5

DISCUSSION

Peritoneal carcinomatosis has long been considered a fatal clinical entity and has been treated palliatively (administration of corticosteroids, therapeutic ascitic aspirations, and surgical bypass). Since the 1980s, there has been a renewed interest in novel therapeutic approaches to peritoneal carcinomatosis. The rationale for IPCH is based on direct cytotoxicity of hyperthermia against malignant cells, enhancement of the cytotoxicity of anticancer drugs, and the pharmacokinetic advantages of the intraperitoneal route for chemotherapy. When combined with cytoreductive surgery, including peritonectomy procedures as described by Sugarbaker,⁵ the results seem promising.⁵ Our pilot study in humans showed that IPCH with MMC and inflow temperatures of approximately 48°C has acceptable morbidity and

TABLE 6. Summary of preoperative and surgical variables and their association with grade III/IV morbidity

Variable	P value
Presence of any complication	
Sex	.502
Age	.509
Carcinomatosis stage	.016 ^a
Primary origin	.920
First or second procedure	.456
Duration of surgery	.005 ^a
Cytoreductive procedure or not	.087
Number of resections and peritonectomy procedures	.042
Number of anastomoses	.070
Completeness of cytoreduction	.183
Digestive fistula	
Carcinomatosis stage	.002
Duration of surgery	<.001
Number of anastomoses	<.001
All other variables	NS

NS, not statistically significant.

^a These variables are significantly associated with the presence of combined grade III/IV morbidity in the multivariate analysis.

mortality rates for selected patients.¹² The toxicity of MMC through the IPCH route is low.^{12,15} In the pilot study of 28 patients, post-IPCH evaluation of serum hematology and biochemistry revealed only a transitory increase in white blood cells and a decrease in platelets, with a return to reference values after the 10th postoperative day. In a prospective phase II study of 83 patients with carcinomatosis from gastrointestinal origin treated by IPCH, we reported acceptable rates of mortality and morbidity: 4% and 10%, respectively.⁴ In light of the poor prognosis of patients with stage 3 and 4 carcinomatosis and the promising survival results published by Sugarbaker and Jablonski,⁷ we decided to combine cytoreductive surgery with IPCH for the comprehensive treatment of patients with carcinomatosis from gastrointestinal or gynecological origin. The combination of these two procedures exposes patients to an increased risk of complications. In our second phase II trial using extensive cytoreductive surgery followed by IPCH for the treatment of digestive carcinomatosis, we reported a morbidity rate of 28.6%.¹⁰ However, this was only 10% in our first trial with IPCH alone.⁴ The present study confirmed that the morbidity rate was higher after the combined approach than after IPCH alone, but without a statistically significant difference.

The morbidity and mortality rates of this study (24.5% and 3.2%, respectively) are comparable to those previously reported by other teams. In a study analyzing 200 treatments with cytoreductive surgery and IPCH with the coliseum technique (open-abdominal technique), Stephens et al.¹⁶ reported morbidity and mortality rates of 27% and 1.5%, respectively. Their morbidity rate included combined grade III/IV morbidity, but all their patients had extensive cytoreductive surgery. In smaller studies, the reported morbidity rates were higher: 38% to 54%.¹⁷⁻²¹ The complication rates decreased with experience. Morbidity should improve through routine use of the optimum hyperthermia procedure, improvements in the composition of the perfusate, and better patient selection. The effectiveness of treatments has remained stable or improved during this evolution, and morbidity has not increased. In the reported study, most of the prolonged ileus occurred in the first years of our experience. Moreover, we no longer include patients with unresectable primary tumors, as we did at the beginning of the study. Three of the seven postoperative deaths were observed in patients who presented with unresectable tumors.

The carcinomatosis stage (or the peritoneal cancer index) has a major prognostic influence on morbidity and survival.^{8,20} Patients with stage 3 or 4 carcinomatosis (malignant granulations >5 mm) had more complica-

tions, digestive fistulas, and systemic sepsis than patients with stage 1 or 2 carcinomatosis (malignant granulations <5 mm). Similar findings were made by Esquivel and Sugarbaker⁸ and Elias et al.,²⁰ who considered that patients with carcinomatosis from colorectal origin with a peritoneal cancer index >20 or 25 are not indicated for the combined therapeutic approach because of their high complication rate and poor prognosis. Stephens et al.¹⁶ found that the peritoneal cancer index had no effect on morbidity or mortality rates. Carcinomatosis stage plays an important role in patient selection. The amount of tumor remaining after cytoreduction may also have an influence on morbidity. CCR-2 patients with large residual tumor volume (tumor nodules >5 mm) had a morbidity rate of 28.3%, whereas it was 20% for CCR-0 or CCR-1 patients with no macroscopic disease or small residual tumor volume. However, this difference was not significant.

As observed by Stephens et al.,¹⁶ the extent of cytoreductive surgery influences morbidity. The number of resections, peritonectomy procedures, and anastomoses and, especially, the duration of surgery, statistically increase the complication rate. It would be expected that morbidity would correlate with the magnitude of surgery. Many patients had moderate to extensive surgery before presenting at our department. They required extensive dissection of all adhesions, stripping of the peritoneum, and organ resections to maximize the benefits of this treatment. Surgical expertise and judgment were required to find a balance between the postoperative risk of extensive surgery and benefit in survival and quality of life. Patients have to be more strictly selected for a second procedure because of the high risk of complications. Even if the statistical analysis did not show a significantly higher morbidity rate after a repeat IPCH than after the first, two of nine patients who underwent a second procedure presented with complications, and one died after surgery.

The digestive fistula rate was 6.5%, and most of these fistulas were the consequence of an anastomotic leakage. Contrary to the teams using the open-abdominal procedure, all our anastomoses had to be fashioned before the perfusion. It does not seem that this influenced the rate of anastomotic leakage, which was comparable to the rates previously reported with the open technique.^{16,17,20} We reported only one spontaneous fistula. To prevent hyperthermia damage to small-bowel surfaces, the inflow drains in which temperatures are higher were inserted under the diaphragmatic cupola and not directly in contact with the intestinal wall. The mean time of occurrence of these fistulas was the 16th postoperative day—later than after conventional gastrointestinal surgery, when

fistulas appear before the end of the second postoperative week. IPCH may be responsible for this delay. Because all the perfusate is not totally discharged with our closed-abdominal procedure, intraperitoneal abscesses may be caused by liquid sequestration in the intraperitoneal cavity, leading to fistula formation. In addition, intestinal tissue and anastomoses are in contact with anticancer drugs for a longer time.

Ten patients (4.6%) demonstrated combined grade III/IV hematological toxicity, and one of these patients died after surgery from aplasia. This hematological toxicity was observed after the use of CDDP. No patient presented with grade III/IV hematological toxicity after IPCH with MMC alone. It is important to note that many patients treated by IPCH with CDDP had chemoresistant ovarian cancer, and 80% of them underwent IPCH and surgery after many courses of systemic chemotherapy and developed bone marrow insufficiency. Pharmacokinetic results of IPCH with MMC have already been reported.^{11,12} The maximum serum concentration of MMC was noticed 45 minutes after the beginning of IPCH, and in every patient, MMC had completely disappeared from plasma within 2 hours and from urine within 24 hours after the end of IPCH.

IPCH by closed-abdominal technique with cytoreductive surgery and peritonectomy procedures is a reasonable treatment for selected patients with carcinomatosis from gynecological and nongynecological malignancies. As reported by Stephens et al.,¹⁶ this combined aggressive therapy has acceptable morbidity and mortality. Strictly selected patients with carcinomatosis, which has, until the advent of cytoreductive surgery and chemotherapy techniques, been uniformly lethal, can be treated effectively in specialized teams. Phase III studies are now necessary to improve selection criteria and survival.

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