Cytoreductive Surgery Followed by Hyperthermic Intraperitoneal Chemotherapy: Morbidity and Mortality Analysis of Our Patients

Sitoredüktif Cerrahi ve Hipertermik İntraperitoneal Kemoterapi: Hastalarımızın Morbidite ve Mortalite Analizi

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ABSTRACT Objective: The purpose of this study was to analyze the morbidity and mortality of cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) and early postoperative intraperitoneal chemotherapy (EPIC) with closed abdomen technique in the treatment of peritoneal surface malignancies. **Material and Methods:** Twenty-six patients (8 with ovarian cancer, 7 peritoneal mesothelioma, 6 colorectal cancer, 3 uterine sarcoma, 1 peritoneal carcinoma and 1 with gastric cancer) underwent 27 procedures. Peritonectomy was performed with complete removal of all the involved visceral and parietal peritoneum. HIPEC was performed with the closed abdominal technique using preheated (42.5°C) perfusate for 60 minutes. EPIC was continued for postoperative 5 days. **Results:** All patients underwent resection of the lesions. Total peritonectomy was performed in 12 patients, while subtotal or partial peritonectomy was carried out in 14 according to the spread of carcinomatosis. Completeness of cytoreduction score of our patients was 0 in 18 patients, 1 in 6 patients and 2 in 2 patients. Major morbidity developed in 7 patients (27%). CRS+ HIPEC+ EPIC yielded acceptable morbidity and mortality rates. Of the 26 patients, 20 (77%) were alive without evidence of disease with a mean follow-up period of 13 ± 6 months. Overall 1 year survival was 60%. **Conclusion:** Cytoreductive approach combined with intraperitoneal chemotherapy prolongs survival in selected patients with peritoneal carcinomatosis (PC) with acceptable morbidity and mortality.

Key Words: Carcinoma; surgery; drug therapy; peritoneal neoplasms

ÖZET Amaç: Bu çalışmanın amacı, periton yüzey malinitelerinin tedavisinde kapalı karın tekniğiyle uygulanan sitoredüktif cerrahi (SRC), hipertermik intraperitoneal kemoterapi (HİPEK) ve erken postoperatif intraperitoneal kemoterapi (EPİK)'nin mortalite ve morbiditesini analiz etmektir. **Gereç ve Yöntemler:** Yirmi altı hastaya (8 over kanseri, 7 peritoneal mezotelyoma, 6 kolorektal kanser, 3 uterin sarkom, 1 periton kanseri ve 1 mide kanseri) 27 işlem uygulandı. Peritonektomi, hastalığın yayıldığı tüm viseral ve parietal peritonun kaldırılmasıyla yapıldı. HİPEK, kapalı karın yöntemiyle 42,5 santigrad dereceye ısıtılmış perfuzat ile 60 dakika süreyle yapıldı. EPİK postoperatif beş gün daha sürdürüldü. **Bulgular:** Tüm hastalarda lezyonlar rezeke edildi. Subtotal veya kısmi peritonektomi, karsinomatozisin yayılma derecesine göre 14 hastada gerçekleştirilirken, total peritonektomi 12 hastaya uygulandı. Hastalarımızın sitoredüktif skorunun toplamı, 18 hastada '0', 6 hastada '1' ve 2 hastada '2' idi. Ağır morbidite 7 hastada (%27) görüldü. SRC + HİPEK + EPİK kabul edilebilir morbidite ve mortalite oranları sergiledi. Yirmi altı hastanın 20'si (%77) 13 ± 6 ay ortalama takip süresi içinde hastalık bulgusu olmadan hayatta idi. Toplam bir yıllık sağ kalım oranı %60 bulundu. **Sonuç:** İntraperitoneal kemoterapi ile kombine sitoredüktif yaklaşım, seçilmiş periton karsinomatozisli hastalarda kabul edilebilir morbidite ve mortalite ile sağkalımı uzatmaktadır.

Anahtar Kelimeler: Karsinom; cerrahi; ilaç tedavisi; peritoneal tümörler

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Peritoneal carcinomatosis (PC) is among the most common routes of dissemination of abdominal neoplasms. Although it may be present at the time of diagnosis of the primary tumor, it arises more commonly as a tumor recurrence after radical surgical treatment.[1] PC is less frequent in colorectal cancer compared to gastric cancer; however, mucinous carcinoma, appendiceal cancer, and cases with positive peritoneal cytology show high rates of peritoneal dissemination.[2]

Peritoneal carcinomatosis originating from nongynecological tumors is generally considered a fatal disease, with a mean survival time of 3-6 months after conventional chemotherapeutic treatments.[3] The most widely accepted therapies for such PC cases are systemic chemotherapy, best support care, and palliative treatment, without any hope of cure. Moreover, surgery alone can only remove the bulky visible tumor burden; for the micrometastases, invisible free cancer cells, and tumors not suitable for resection, surgery has no effect. Therefore, neither surgery nor chemotherapy alone can make an obvious difference in terms of quantity and quality of life in patients with PC.[4]

In the last years, some centers have reported encouraging results with hyperthermic intraperitoneal chemotherapy (HIPEC).[3] HIPEC combines the direct effects of hyperthermia against the tumor cells with the effects of locoregional chemotherapy; anticancer activity of several chemotherapeutic agents and their tissue penetration is also enhanced by hyperthermia. Surgical procedures, including debulking of abdominal tumor mass, resection of organs invaded by primary tumors and partial or total peritonectomy are often combined with HIPEC in order to reduce tumor volume.[5]

In this study, we reported the results of our experience with this type of treatment, with special reference to postoperative outcome and potential risk factors for morbidity.

MATERIAL AND METHODS

From September 2007 to June 2010, 26 patients with PC have been treated with cytoreductive surgery (CRS) + HIPEC + early postoperative intraperitoneal chemotherapy (EPIC) at the Department of General Surgery, Cumhuriyet University Faculty of Medicine. The patients included 8 cases with ovarian cancer, 7 with peritoneal mesothelioma, 6 with colorectal cancer, 3 with uterine sarcoma, 1 with peritoneal carcinoma, and another with gastric cancer.

Preoperative evaluation always included a thoracic and abdominal computed tomography (CT) scan to stage peritoneal disease and exclude distant metastases. General condition of the patients was carefully assessed including complete blood tests, electrocardiogram, cardiac ultrasound examination and spirometry. Informed consent was obtained from all patients. Major clinicopathological characteristics of the patients were listed in Table 1.

Abdominal exploration was performed under general anesthesia and hemodynamic monitoring through a midline xiphoid-pubic incision. Peritoneal Cancer Index (PCI) of Sugarbaker was chosen by an expert panel.[6] When the PCI evaluation was over, maximal CRS was performed, including the resection of the primary tumor with acceptable margins, any involved adjacent structures, lymphadenectomy, and peritonectomies where peritoneal surfaces were invaded by tumor, according to previously published surgical guidelines.[7] The extent of CRS was determined by

TABLE 1: Clinicopathologic characteristics of 26 patients with peritoneal carcinomatosis.

Characteristic	Value
Demographic parameters	
Age range (median) (years)	22-80 (53.2)
Sex (M/F)	6/20
Clinicopathological parameters (n)	
Ovarian cancer	8
Peritoneal mesothelioma	7
Colorectal cancer	6
Uterine sarcoma	3
Gastric cancer	1
Peritoneal carcinoma	1
Peritoneal carcinomatosis index (range) (mean)	16-24 (18.5)
Completeness of cytoreduction	0 in 18 patients, 1 in 6 patients, 2 in 2 patients.

F, female; M, male.

previously published criteria on the Completeness of Cytoreduction (CCR).[7] A CCR score of 0 indicates no residual peritoneal disease after CRS; 1 represents <2.5 mm of residual disease; 2 indicates residual tumor between 2.5 mm and 2.5 cm; and 3 indicates >2.5 cm of residual tumor or the presence of a sheet of unresectable tumor nodules.[7]

After cytoreduction, four drainage tubes were placed at four major abdominal quadrants. Abdomen was closed and HIPEC was performed through closed abdominal technique. This technique was conducted with preheated (42.5 °C) perfusate (3 L of saline solution) containing chemotherapeutic agents as described in Table 2 for 60 minutes. The perfusion solution was infused into the peritoneal cavity at 300 mL/min through the inflow tube introduced from an automatic perfusion pump. (COBE perfusion system, Denver, USA) (Figure 1). Other tubes were functioned as an outflow tube. The first 1 L of the perfusion solution was discarded through a drainage tube to wash out the residual debris and detached tumor cells, and the remaining solution (3 L) that contained chemotherapeutic agents was kept to circulate in the perfusion system.

HIPEC was followed by EPIC. During postoperative days 1-5, described chemotherapeutic agents (Table 2) were administered into the peritoneal cavity in 1 L saline solution. After 23 hours, this solution was drained outside by opening the abdominal drains for 1 hour. After drainage, the new solution with agents was administered to the abdominal cavity and this procedure was repeated for 5 postoperative days. All patients received EPIC. For uterine sarcoma, ovary, gastric and colorectal cancer patients, further systemic chemotherapy was administered as clinically indicated.

POSTOPERATIVE MONITORING AND FOLLOW-UP

At the end of the operation, patients were admitted to the intensive care unit for at least 48 hours and then were returned to the surgery department when cardiovascular and pulmonary functions became stable. Continuous monitoring of hepatic and renal functions and hydroelectrolytic balance was carried out afterwards. Pulmonary cardiovascular functions were also monitored. Antibiotic and thromboembolic prophylaxes were administered to all patients.

Data of the patients were obtained from a database of clinical records, surgical reports, medical imaging reports, laboratory and pathology reports, and follow-up records. All patients were routinely followed-up in the outpatient clinic or by telephone and the information was recorded. The last follow-up was on June 1, 2010. The survival time was calculated from the date of first CRS + HIPEC+ EPIC to the date of patient death due to any cause.

RESULTS

All patients (n= 26) underwent resection of the lesions as described in Table 3. Eleven patients had been previously operated for various types of carcinoma. Fourteen patients had gastrointestinal system resection requiring anastomoses. While in 9 of those anastomoses were performed, 5 underwent ileostomy.

Peritoneal Cancer Index range (mean) of our patients was 16-24 (18.5) (Table 1). Total peritonectomy was performed in 11 patients, while

TABLE 2: Intraperitoneal Hyperthermic Perfusion (HIPEC) and Early Postoperative Intraperitoneal Chemotherapy (EPIC) protocols.

Pathology of the patients	HIPEC protocol	EPIC protocol
Peritoneal mesothelioma or Ovarian cancer	Cisplatin (30 mg/m^2) + Mitomycin C (20 mg/m^2)	Paclitaxel (20 mg/m^2/day) Protocol of day 1-5.
Uterine sarcoma	Cisplatin (30 mg/m^2) + Mitomycin C (20 mg/m^2)	5-FU* (600 mg/m^2/day) (Protocol of day 1-5)
Colorectal cancer or Gastric cancer	Cisplatin (30 mg/m^2) + Mitomycin C (20 mg/m^2)+ 5-FU (600 mg/m^2/day)	5-FU (600 mg/m^2/day) + mitomycin C (20 mg/m^2) (Protocol day 1) 5-FU (600 mg/m^2/day) (Protocol day 2-5)

*5-FU (5-Fluorouracil).

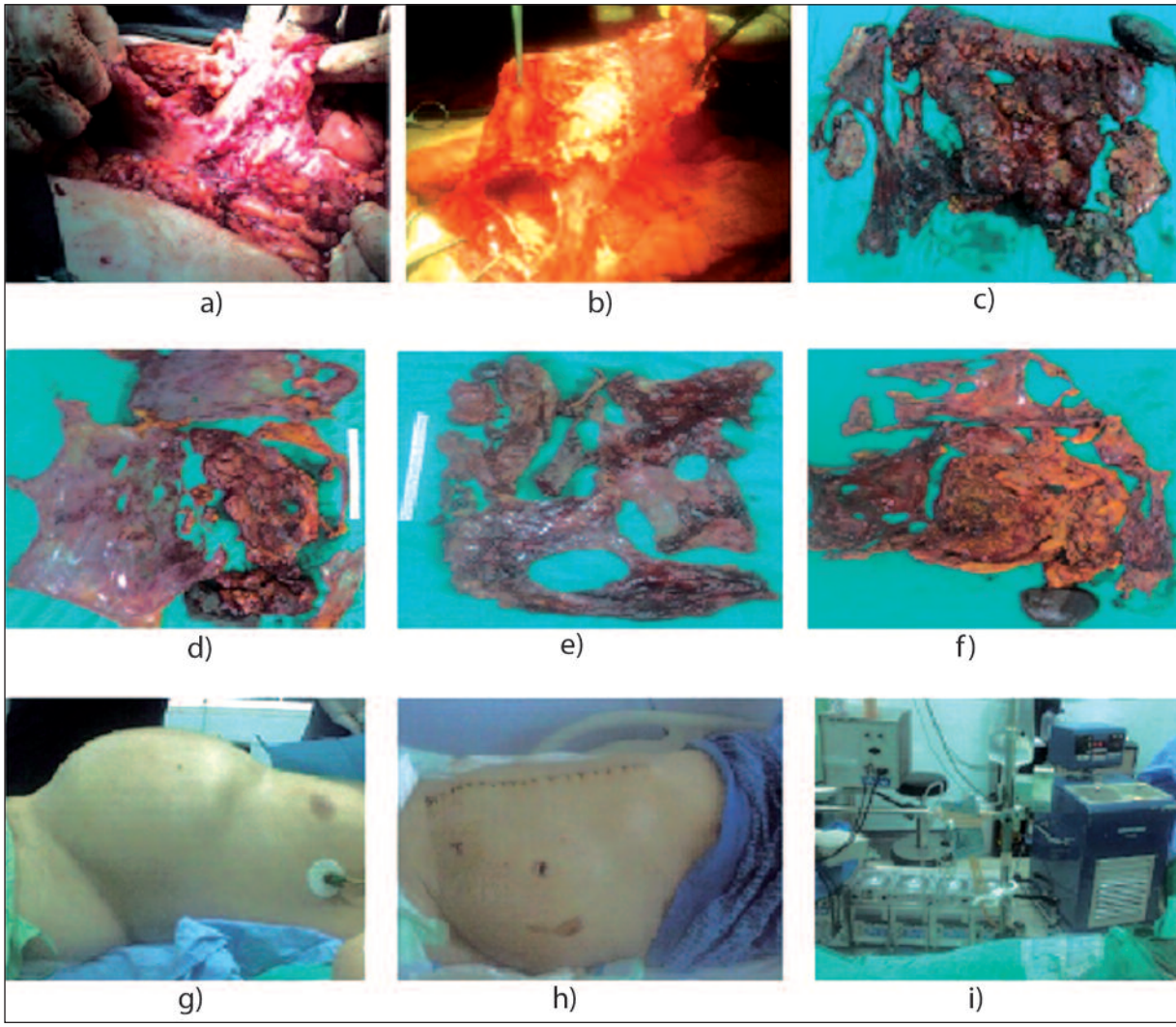

FIGURE 1: a) Peritoneal carcinomatosis in one patient. **b)** Peritonectomy procedure. **e c,d,e,f)** Resected specimens after cytoreductive surgery. **g,h)** Malignant ascite of one patient that resolved after cytoreductive surgery. **i)** Perfusion system for HIPEC.
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subtotal or partial peritonectomy was carried out in 15 patients according to the extent of carcinomatosis. Completeness of cytoreduction score in our patients was 0 in 18 patients, 1 in 6 patients and 2 in 2 patients (Table 1). The time of surgery ranged from approximately 5-7 h (median 6 h, mean 6 ± 0.5 h).

Mean hospital stay was 12 ± 5 (range 8-28) days. The volume of blood loss during surgery was 700 to 4000 mL, blood transfusion was 700 to 2400 mL, and fluid infusion was 2000 to 7500 mL.

Among the 26 patients, 3 had aspartate aminotransferase levels >46 U/L after surgery and in other 3 patients blood urea nitrogen and creatinine levels increased to 50 ± 9 mg/dL and 2.2 ± 0.5 mg/dL respectively; the levels of all tests improved within a few days. Five patients developed hypoproteinemia, but other laboratory results were normal.

POSTOPERATIVE COMPLICATIONS

Morbidity rate was calculated based on postoperative complications that developed during the hospital stay or within 30 days following surgery; overall, 12 complications developed in this series (morbidity rate 46%). All complications were listed in Table 4. Wound infection (n= 3), pleural effusion (n= 1) and gastric atonia (n= 2) were considered

TABLE 3: Characteristics of the patients.

Patient no.	Age(years)	Sex	Diagnosis	PCI	Previous surgery	PROCEDURE (... +HIPEC+EPIC)	CCR	Complication	Treatment	Survival status
1	22	F	Colon cancer	16	-	BSO + Right colectomy + Pelvic peritoneum resection	0	-	-	SWOT 31 months
2	58	F	Ovarian cancer	18	-	TAH + BSO + Splenectomy + Total omentectomy + Appendectomy + Intraabdominal tumor total resection + Pelvic peritoneum resection	0	-		SWOT 31 months
3	46	F	Ovarian cancer recurrence in abdomen	20	TAH+BSO+ Pelvic, paraaortic lymph node dissection	Distal pancreatectomy + Splenectomy + Cholecystectomy + Omentectomy + Low Anterior Resection + Total peritonectomy	0	Hematological toxicity (leukopenia)	Medical	SWOT 23 month
4	48	F	Ovarian cancer	20	-	TAH + BSO + Pelvic, paraaortic lymph node dissection Total peritonectomy + Omentectomy + Appendectomy	1	Wound infection	Drainage	SWOT 20 months
5	57	F	Peritoneal papillary serous carcinoma	22	-	Subtotal colectomy + Ileoproctostomy + Ileum resection + Resection of right upper and lower quadrant of the abdominal peritoneum	0	Intra abdominal sterile fluid collection	CT-guided percutaneous drainage	SWOT 20 months
	60	F	Uterine sarcoma	20	-	TAH + BSO + Total omentectomy + Appendectomy Splenectomy + Cholecystectomy + Pelvic peritonectomy	0	-	-	SWOT 18 months
6	49	M	Peritoneal mesothelioma	24	Laparotomy + biopsy	-Total colectomy + Small bowel resection + Ileoostomy+ Omentectomy + Splenectomy + Total peritonectomy	1	Gastric atonia	Medical	SWOT 18 months
7	56	M	Colon cancer	18	-	Sigmoid colon resection + Partial small bowel resection + Resection of left anterior and pelvic peritoneum	0	-		SWOT 18 months
8	54	M	Peritoneal mesothelioma	24	Laparotomy + biopsy	Total peritonectomy	2	-	-	SWOT 18 months
9	56	F	Ovarian cancer	18	-	TAH + BSO + Total omentectomy + Appendectomy + Paraaortic lymph node dissection + Pelvic peritoneum resection	0	-	-	SWOT 18 months
10	62	F	Recurrent uterine sarcoma	24	TAH+BSO	Total colectomy + Omentectomy + Splenectomy + Distal gastrectomy + Ileostomy + Left diaphragmatic peritoneum resection	2	-	-	SWOT 18 months
11	36	F	Gastric cancer	20	-	Total gastrectomy + Cholecystectomy + TAH + BSO + Pelvic peritoneum resection	1	Oesophagojejunal fistula	Medical	SWOT 9 months, SWOT 3 months death in month 12 due to recurrence
12	72	M	Peritoneal mesothelioma	18	Laparotomy + biopsy	Splenectomy + Omentectomy + Appendectomy + Total peritonectomy	0	-	-	SWOT 14 months
13	62	F	Colon cancer recurrence in abdomen	18	Right hemicolectomy	Intraabdominal tumor total resection + Omentectomy + Left upper and lower quadrant peritoneum resection and pelvic peritonectomy	0	-	-	SWOT 14 months
14	52	F	Peritoneal mesothelioma	18	TAH+BSO	Total colectomy + Omentectomy + Splenectomy + Total gastrectomy + Total peritonectomy + Ileostomy	0	Acute renal failure	Medical	SWOT 14 months
15	50	M	Peritoneal mesothelioma	20	Laparoscopic biopsy	Total colectomy + Omentectomy + Splenectomy + Cholecystectomy + Ileostomy + Total peritonectomy	1	Intraabdominal bleeding	Medical	SWOT 14 months

→continued

TABLE 3: *continued.*

16	69	F	Colon cancer	20	-	Total colectomy + Ileostomy TAH + BSO + Total peritonectomy	1	Wound infection	Drainage	Exitus 7 months later due to disease progression
17	57	F	Ovarian cancer	18	TAH+BSO+ omentectomy	Total colectomy + Splenectomy + Cholecystectomy + Ileostomy + Total peritonectomy	0	-	-	SWOT 10 months
18										
19	48	F	Recurrent colon cancer	18	Sigmoid resection	Omentectomy + Partial small bowel and recurrent intraabdominal mass resection + Left lower quadrant and pelvic peritoneum resection	0	-	-	SWOT 10 months
20	59	F	Peritoneal mesothelioma	18	Laparotomy + biopsy	Splenectomy + Omentectomy + Appendectomy + Cholecystectomy + Total peritonectomy	0	-	-	Exitus 3 months after the operation due to brain metastases
21	80	F	Uterine Sarcoma	20	-	TAH + BSO + Total colectomy + Splenectomy + Omentectomy + Pelvic peritoneum resection	1	Intestinal fistula,	Second operation was performed due to fistula and anastomosis was changed to terminal ileostomy.	Exitus 30 days after the operation due to cardiovascular problems
22	60	F	Ovarian cancer	18	-	TAH + BSO + Total omentectomy + Appendectomy + Splenectomy + Meckel diverticulum excision + Pelvic peritonectomy + Pelvic, paraaortic lymph node dissection	0	Pleural effusion, Intra abdominal sterile fluid collection	Percutaneous drainage	Exitus on postoperative day 27 due to pulmonary problems
23	54	F	Ovarian cancer	20	-	TAH + BSO + Total omentectomy + Pelvic peritoneum resection	0	-	-	SWOT 6 months
24	44	F	Colon cancer	18		Total colectomy + Omentectomy + Anterior abdominal wall mass resection + Partial peritonectomy + Ileostomy	0	Wound infection	-	Exitus 4 months later due to internal fistula+ sepsis
25	60	M	Peritoneal mesothelioma	18	-	Total peritonectomy + Omentectomy	0	-	-	SWOT 5 months
26	67	F	Ovarian cancer	20	-	TAH + BSO + Partial peritonectomy	0	-	-	SWOT 5 months

CCR: Completeness of cryoreduction; PCI: Peritoneal carcinomatosis index; SWOT: Survival without tumor; SWT: Survival with tumor; TAH+BSO: Total Abdominal Hysterectomy+Bilateral Salpingooferectomy.

TABLE 4: List of postoperative complications that developed in 26 patients.

Complication	No. of cases	Treatment
Wound infection	3	Drainage
Gastric atonia	1	Medical
Pleural effusion	1	Percutaneous drainage
Intraabdominal sterile fluid collection requiring drainage	2	CT-guided percutaneous drainage
Intestinal fistula	2	One with medical, Other one reoperated and anastomosis was changed to terminal ileostomy.
Acute renal failure	1	Medical
Intraabdominal bleeding	1	Medical
Hematological toxicity (Leukopenia)	1	Medical
Total	12	

CT, computed tomography.

minor complications. Major complications developed in 7 patients (27%), including intestinal fistula (n= 2), intraabdominal sterile fluid collection (n= 2), acute renal failure (n= 1), intraabdominal bleeding (n= 1) and hematological toxicity (n= 1).

Two patients with intraabdominal sterile fluid collection underwent CT-guided drainage and percutaneous drainage was performed for pleural effusion of another patient. While one case with intestinal fistula was resolved with medical treatment in ten days, the other case underwent a second operation and anastomosis was changed to terminal ileostomy. One case with acute renal failure was resolved by medical therapy within a few days without dialysis. One case had intraabdominal bleeding in the postoperative period. Bleeding continued on postoperative day 2 and resolved after medical therapy. In this patient EPIC was initiated on postoperative day 4. Hematological toxicity (leukopenia) of one patient lasted for 1 week and was managed with medical therapy.

One patient died on postoperative day 27 due to pulmonary problems and other patient died 30 days after the operation due to cardiovascular problems (mortality rate 7.6%).

SURVIVAL

The last follow-up was on November 1st, 2010, either at the outpatient clinic or by telephone. The follow-up time ranged from 27 days to 31 months for all patients (n= 26). Of the 26 patients, 20 (77%) were alive without evidence of disease with a mean follow-up of 13 ± 6 months. Overall 1 year survival rate was 60%.

Three patients died of disease progression, one due to gastric carcinoma widespread metastases to the abdominal cavity, one due to colon cancer widespread metastases to the abdominal cavity with 7-month survival and one due to malignant peritoneum mesothelioma metastases to brain with 3-month survival. One patient died at four months after the operation, due to internal fistula + sepsis.

DISCUSSION

The comprehensive management plans include surgery to remove large-volume disease within the abdomen and pelvis and perioperative intraperitoneal chemotherapy to eradicate microscopic residual disease. HIPEC associated with cytoreductive surgery is becoming a widely accepted procedure for the prevention or treatment of PC due to abdominal cancer.[3] This indication is based upon the concept that PC may be considered a locoregional condition not necessarily associated with systemic dissemination of the disease. Several biological and clinical studies support this hypothesis.[8] Many phase I and II studies have been conducted with promising results and this new treatment modality has gained increasingly wide acceptance in the treatment of PC.[7-10]

To achieve effective cytoreduction, the area of surgery should be wide and multiple organ parts may be resected. This leads to a high risk of major postoperative complications such as digestive fistu-

las and generalized sepsis in particular, with a morbidiy rate ranging from 14% to 55% and a mortality ratet between 0% and 19%.[7-10] Major morbidity and postoperative mortality of this series was 27% and 7.6% respectively; which are similar to the incidence reported by specialized centers.[8-11]

The main morbidity of cytoreductive surgery combined with HIPEC is due to complications of surgery such as anastomotic leakages, intraperitoneal sepsis, or abscesses.[12] Wound infections (n= 3) and intestinal fistula (n= 2) were the most common causes of morbidity in our patients. Intestinal fistula has been reported to be an important cause of morbidity and mortality in patients submitted to HIPEC, with an incidence rate ranging from 6% to 27%.[10-13] HIPEC has a detrimental effect on the strength of visceral anastomosis and in patients submitted to HIPEC, even nonresective procedures can be associated with intestinal fistula in the postoperative period.[11-14] While one of the patients with anastomosis leakage in this series was managed with medical management, the other patient needed reoperation and the anastomosis was changed to terminal ileostomy. The second principal morbidity due to HIPEC is hematological toxicity, which is reported to occur in 8% to 31% of cases.[12] We detected this problem in one patient and managed succesfully with medical treatment.

Recent studies have reported the duration and extent of surgery, visceral resections, carcinomatosis stage and incomplete cytoreduction as important risk factors for postoperative complications after Cytoreductive Surgery (CRS) and HIPEC.[13,14] Two deaths developed, one due to pulmonary problems and the other to cardiovascular problems. Both patients had very advanced diseases and old age and required long operative time. Like reports in several studies, the results of our experience with HIPEC indicate that, even when combined with an aggressive surgical procedure, this technique is associated with an acceptable risk of postoperative complications and mortality.[10-14]

In 2004, Glehen et al. published a large-scale multicentric prospective study involving 506 patients who underwent CRS + HIPEC from 28 centers.[15] The average follow-up was 53 months; the mean survival time was 19.2 months; and the 1, 3, and 5-year survival rates were 72%, 39%, and 19%, respectively. Thirty-eight patients survived for >5 years. The follow-up period of this series was 27 days to 31 months for all patients (mean 13±6 months). Twenty patients (77%) were alive without evidence of the disease (Table 3). They experienced disease-free survival with a satisfactory performance status. Overall 1 year survival was 60%.

Completeness of Cytoreduction (CRS) is a strong determinant of outcome in patients treated with HIPEC.[10-15] The patients with optimal CRS followed by HIPEC showed the best 5-year survival rate of 30%, whereas those underwent incomplete CRS gained little benefit, with a median survival comparable to that reported in historical controls.[11-17] Completeness of cytoreduction score in our patients was 0 in 18 patients, 1 in 6 patients, and 2 in 2 patients. In most of our patients complete cytoreduction was obtained, which is indicative of appropriate patient selection. Among the 6 patients who died, the CCR scores were 1 in 3 patients. Therefore, we think that better scores for completeness of cytoreduction affects the survival positively.

Despite CRS, the disease recurrence rate is still high, leading to treatment failure. In a multi-institutional study by Glehen et al, the overall incidence of recurrence was 73.3%.[16] In a prospective study by Bijelic et al, among 70 patients with colorectal cancer undergoing combined treatment, 49 developed documented recurrence at a median time for progression of 9 months, and most recurrent disease occurred inside the abdomen.[17] One possible cause for such a high failure rate could be the marked differences in drug sensitivity between different PC types and between individuals with the same tumor types, as was found in a recent study of PC samples.[18] Therefore in the future, we are planning to perform in-vitro chemosensitivity directed (Tailored) adjuvant chemotherapy. We detected recurrence in 4 (15%) of our patients (Table 3).

Incidence for **peritoneal** mesothelioma in this series (n= 7) was higher than in other reports.[4,18-21] This may be due to the closeness of our University

Hospital to epidemic areas **Cappadocia** and Yıldızeli, which are rich in **erionite**, a **zeolite** mineral with similar properties to **asbest**. In Cappadocia, an unprecedented mesothelioma epidemy caused 50% of all deaths in three villages. The treatment modality used in this study may be beneficial for people living in those areas.

In conclusion, CRS and HIPEC + EPIC were well tolerated in our patients with PC, some of whom had improved survival. The combination of extensive surgery and intraperitoneal chemotherapy should be the treatment of choice in specialized centers involved in the management of peritoneal surface malignancies.

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