EJGO European Journal of Gynaecological Oncology

Cytoreductive surgery and perioperative intraperitoneal chemotherapy for gynecological malignancies: a single center experience

K. Karadayi[1,2], C. Yildiz[3], S. Karakus[3], O. Bozoklu Akkar[3], G. Pakay Ugurlu[3], A. Kurt[1], A. Yanik[3,4]

[1] Departments of [1] General Surgery, [2] Division of Surgical Oncology, and [3] Obstetrics and Gynecology, [4] Division of Gynecologic Oncology, Cumhuriyet University School of Medicine, Sivas (Turkey)

Summary

Introduction: The objective of this study was to assess the outcome of cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) plus early postoperative intraperitoneal chemotherapy (EPIC) in patients with advanced gynecological malignancies. *Materials and Methods*: A retrospective series of 51 patients with advanced gynecologic cancer, evaluated between May 2008 to February 2014. Peritoneal Cancer Index (PCI) and Completeness of Cytoreduction (CCR) score were used in the study group. The study group consisted of the cancers of ovarian, fallopian tube, endometrial, and uterine sarcomas. *Results*: Mean PCI score of the study group was 18, and the postoperative complications were similar with the literature. Patients were followed in a period of 15 days to 64 months and the mean survival time was 22.8 months. Fifty-two percent of the patients were alive without evidence of the disease and overall one-year survival was found 56%. *Conclusions*: The authors concluded that CRS, HIPEC, EPIC, and peritonectomy are a crucial options in patients with advanced gynecological cancers.

Key Words: Cytoreductive surgery; HIPEC: EPIC; Peritonectomy.

Introduction

In the management of cases with peritoneal carcinomatosis (PC) due to gynecological malignancies, cytoreductive surgery (CRS) and perioperative intraperitoneal chemotherapy (IPC) have been used increasingly [1-4]. In these cases, peritoneal implants are the main factors for the failure of surgical management. Cytoreduction can increase survival if extensive resection is performed successfully. In this context, addition of peritonectomy has been accepted as an important component of debulking surgery [5, 6]. Although previously considered incurable by standard oncological surgery, patients with peritoneal metastases are now being given a second chance to survive with CRS plus hyperthermic intraperitoneal chemotherapy (HIPEC) and early postoperative intraperitoneal chemotherapy (EPIC).

IPC regimens include HIPEC and EPIC. The term of HIPEC describes the IPC that is used in the operating room in hyperthermia, and EPIC, which is administered in normothermia, describes the extending of the period of IPC beyond the operating room. HIPEC done promptly after peritonectomy maintains a better dissemination of the chemotherapeutics between peritoneal layers because of the hyperthermia, thus provides a better influence in the residual peritoneal implants when compared to delayed intraperitoneal infusion chemotherapy [7]. It was demonstrated that combined use of CRS plus HIPEC plus EPIC provides better disease-free and overall survival than palliative-intent surgery and/or systemic chemotherapy [8-11].

Since the introduction of use of CRS, HIPEC, and EPIC together, multiple studies have been published about their complications and outcome. They demonstrated that in selected cases this treatment modality improved survival in PC. Most of these studies are related to gynecological malignancies with PC. According to the authors' knowledge, there is no study assessed clinical contribution of combined use of CRS and IPC regimens in this population. They aimed to share their experience with 51 patients who underwent combined use of CRS and IPC regimens in the present institution and to examine their complications and outcome.

Materials and Methods

The authors performed a retrospective review of all cytoreductive surgery plus HIPEC plus EPIC administrations in patients with gynecological cancer. The study protocol was approved by the Human Ethics Committee of the present University and then written informed consent was obtained from each subject enrolled in this study. In a period from May 2008 to February 2014, the authors collected the clinical data of 51 patients who underwent CRS plus HIPEC plus EPIC procedures for the management of advanced gynecologic cancer. The age, primary tumor type, complication type, and outcome of the study population were recorded. Peritoneal Cancer Index (PCI) was

Revised manuscript accepted for publication November 10, 2014

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
XXXVII, n. 2, 2016
doi: 10.12892/ejgo2786.2016

7847050 Canada Inc.
www.irog.net

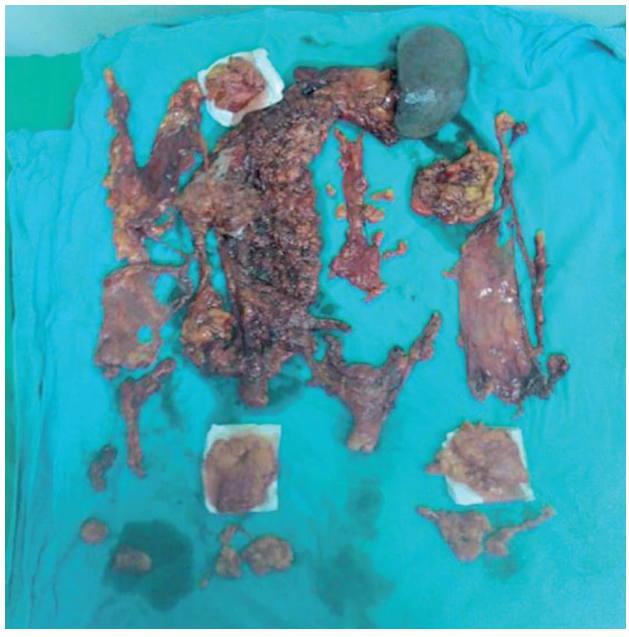

Figure 1. — Surgically resected tissues after the completeness of surgical procedure.

used to evaluate the peritoneal dissemination and the residual disease was evaluated with the Completeness of Cytoreduction score (CCR) [12]. Exclusion criteria were: history of abdominal radiotherapy, detection of extra-abdominal metastases, and a concomitant malignancy of non- gynecologic origin.

Surgical procedure

After the PCI evaluation was completed, maximal CRS was performed, including the resection of the primary tumor with acceptable margins, any involved adjacent structures, lymphadenectomy, and peritonectomy where peritoneal surfaces were invaded by tumor, according to previously published surgical guidelines [13] (Figure 1). Hysterectomy, salpingo-oophorectomy, and pelvic-para-aortic lymphadenectomy procedures were performed in all of the patients as routine gynecological surgery.

Implants on all peritoneal surfaces were excised by electrocoagulation. PCI, ranging from 0 to 39 that increased with the severity of the disease, was performed at the beginning of the surgery in order to evaluate the dissemination of the disease [14-16]. CCR was based on Sugarbaker's criteria that consists of CCR0 (no residual tumour); CCR1 (residual tumour < 2.5 mm); CCR2 (residual tumour 2.5 - 25 mm), and CCR3 (residual tumour > 25 mm) [17].

Mean hospital stay was 12 ± 5 (range 8-29) days. The volume of blood loss during surgery was 700 to 4500 ml, blood transfusion was 700 to 2500 ml, and fluid infusion was 2,500 to 7,000 ml.

Peritonectomy procedure

All tumoral implants were removed by stripping the peritoneum using electrocoagulation. Local excision was performed for small implants on the serosa of the small intestine and colon; however, in order to enhance the effect of perioperative intraperitoneal chemotherapy, all visible tumors were resected. Pelvic peritonectomy was performed by peritoneal stripping of lower abdominal wall, pelvic side wall and resection of the sigmoid colon, and mesosigmoid colon from the origin of the inferior mesenteric artery [18]. The peritoneum of the inner surface of the anterior abdominal wall and diaphragmatic surface were dissected as a part of total peritonectomy at appropriate patients. The greater omentum was removed to prevent the recurrence, even if there was no visible tumour.

Table 1. — *Clinicopathological features of the study patients.*

Parameters	
Age, years	57.5 (19-80)
Primary tumor type	
Ovarian	28 (54.9)
Fallopian tube	17 (33.3)
Endometrial	4 (7.8)
Uterine sarcoma	2 (3.9)
Total	51 (100.0)
Peritoneal cancer index	18 (9-39)

HIPEC and EPIC procedures

In HIPEC procedure after cytoreductive surgery, four drains were placed into the peritoneal cavity and connected to a closed extracorporeal sterile circuit. Four to six L of perfusate including cisplatin 30 mg/m2 and paclitaxel 20 mg/m2 was given through the peritoneal cavity for 60 minutes. The perfusate was heated to target temperatures between 42 and 43ºC [19-21].

In EPIC procedure, paclitaxel 20/mg/m2/day was administered into the peritoneal cavity in one-L saline solution. After 23 hours, this solution was drained outside by opening the abdominal drains for one hour. After drainage, the new solution with paclitaxel was administered into the abdominal cavity and this procedure was repeated for first five days in postoperative period [12]. After the completion of EPIC, appropriate systemic chemotherapy regimens were administered in all the patients.

Statistical analysis

Descriptive statistical analysis was used to summarize the variables. Data are presented as median (min-max) and percentage as appropriate. Survival analysis was applied by the Kaplan-Meier method.

Results

Clinicopathological features of the patients are listed in Table 1. In the study population, the age ranged from 19 to tears, although its median value was 57.5 years. Majority of the patients had ovarian cancer, followed by in order of frequency as fallopian tube, endometrial, and uterine sarcomas. The mean value of PCI was found 18 in the patients of this study. CCR score was found 0 in 40 patients, one in seven patients, and two in four patients. Cytoreduction could not be performed in three patients because of advanced peritoneal involvement and severe intraoperative hypotension in one patient.

Additional surgical procedures performed after routine gynecological surgery are listed in Table 2. Appendectomy was performed in more than half of the patients. Total omentectomy was performed more than infracolic omentectomy (83.3% *vs.* 14.6%). The rates of total and pelvic

Table 2. — *Additional surgical procedures after routine gynecological surgery.*

Surgical procedures	n (%)
Appendectomy	28 (54.9)
Omentectomy	
Total	40 (78.4)
Infracolic	7 (13.7)
Cholecystectomy	9 (17.6)
Peritonectomy	
Total	30 (58.8)
Pelvic	19 (37.2)
Anterior parietal	2 (3.9)
Small bowel resection (partial)	11 (21.5)
Splenectomy	
Total	7 (13.7)
Partial	2 (3.9)
Colectomy	
Total	6 (11.8)
Subtotal	4 (7.8)
Anterior resection	4 (7.8)
Left hemicolectomy	5 (9.8)
Right hemicolectomy	6 (11.8)
Ileostomy	12 (23.5)
Colostomy	4 (7.8)
Gastrectomy	
Total	2 (3.9)
Distal subtotal	3 (5.9)
Liver resection	
Wedge	3 (5.9)
Radiofrequency ablation	2 (3.9)
Segmentectomy	3 (5.9)
Distal pancreatectomy	1 (2)
Adrenalectomy	1 (2)

Table 3. — *Postoperative complications.*

Complication	n	Treatment
Jejunal perforation	1	Surgical*
Intestinal fistula	2	Surgical
Anastomotic leakage	2	Surgical
Pelvic abscess	1	Drainage
Surgical site infection	6	Drainage, medical
Gastric atony	4	Medical
Intra-abdominal fluid collection	2	Drainage
Pleural effusion	4	Drainage
Bone marrow toxicity	1	Medical

*The patient was dead after surgery for complication.

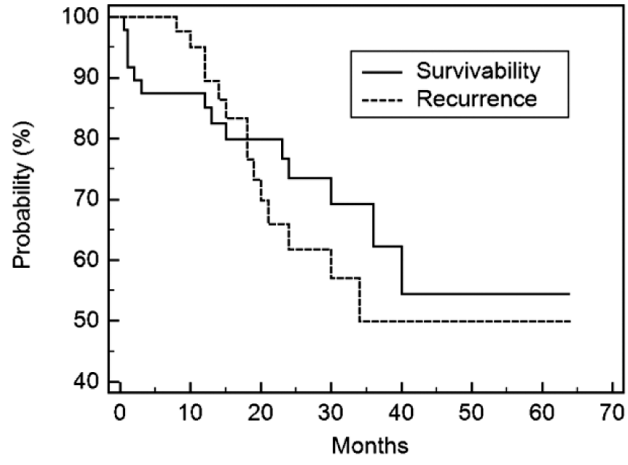

Figure 2. — Survivability and recurrence of study population.

peritonectomy procedures were similar (41.7% *vs.* 56.3%). The other surgical procedures were performed in 4.2-18.8% of the patients.

Postoperative complications are presented in Table 3. Of 51 patients, 22 had surgical complications and one had bone marrow toxicity related to IPC. Jejunal perforation developed in one patient and the patient is dead after the surgery for this complication.

Figure 2 displays the survivability and recurrence probabilities of the study population. Overall, the survivability was decreased gradually to 55% until 40 months and there was a parallel decrease in the probability of recurrence.

Discussion

The authors analyzed the outcomes of 51 patients with advanced gynecologic cancer who underwent extensive cytoreductive surgery plus perioperative IPC regimens. More than half of the patients (54.9%) had a diagnosis of advanced ovarian cancer. Most of the patients with ovarian carcinoma were diagnosed in the advanced stages of the disease, because the disease has no specific symptoms in its early stages [22]. In this study intestinal fistula (n=2) and anastomotic leakage (n=2) were the major causes of morbidity. Intestinal fistula has been accepted as a major cause of the morbidity and mortality for CRS and IPC regimens, with an incidence rate ranging from 6% to 27% [23, 24]. Intestinal fistula may occur due to the adverse effect of chemotherapeutic agent on wound healing of anastomosis that is performed after the resection of intestine. The other causes of intestinal fistula may be due to the lysis of tumor nodules that are involved in full thickness of intestines by intraperitoneal administration of chemotherapy agents, high temperature of the inflow catheter, mechanical or thermal damage of the outflow catheter on the intestinal surface. In the present series, complication of intestinal fistula is relatively low. The authors think that the low rate of this complication is due to performing the prophylactic stoma (ileostomy/colostomy). They also think that gastric atony occurs secondary to total omentectomy. When total omentectomy and splenectomy were performed together, they ligated the branches of right and left gastroepiploic vessels over entrance to the stomach and the short gastric vessels, therefore the greater curvature of the stomach has been

skeletonized. This condition may be responsible from gastric atony. In the treatment of this complication the authors use nasogastric drainage for seven to ten days. Pleural effusion may be due to the transition of the chemotherapeutics to the thoracic cavity with the negative pressure effect after the diaphragmatic stripping or pleural damage. In cases with diaphragmatic resection or pleural damage, the authors recommend the insertion of a chest tube after routinely repairing the diaphragm. Fluid collection in the abdomen occurred in four patients. Microbiological culture of this fluid was negative and cytological examination showed no malignant cells. This condition is determined as sterile fluid collection in the literature [25]. This complication may be due to the collection of the chemotherapeutic agent because of the early postoperative intra-abdominal adhesions or the lack of adequate drainage of the chemotherapeutic agent during IPC. The authors managed this complication with computerized tomography-guided drainage. Chemotherapy or splenectomy may cause hematologic changes. If the spleen is not involved in the cancer, splenectomy is not recommended and partial splenectomy should be done when the involvement of the spleen is local [26]. Although the high PCI of the present study group, the survivabilities of the present patients were similar with the literature, and the authors think that this condition is associated with the low CCR score of the study group. The high PCI may be due to low socioeconomic status of the patients.

Platin and taxol-containing chemotherapy following CRS is the major treatment in cases of advanced ovarian cancer, and with this treatment modality, there is a high rate of complete response in 70-80% of the patients. However, only 30% of patients with complete response reach five-year survival, and 47% of them relapse within five years [27]. Chemotherapeutic agents for IPC varies in the literature. The present authors used the combination of paclitaxel (20 mg/m^2/day) and cisplatin (30 mg/m^2). In case of ovarian cancer treatment including cytoreduction and perioperative intraperitoneal chemotherapy should be performed extensively, aiming to improve the quality of life and survival of the patient [12]. Griffith *et al.* [27] discovered an inverse relationship between residual tumor load and survival in 1975, thus CRS is the preferred method of treatment in cases with advanced ovarian cancer. Recent studies showed that, increase in the survivability of the patients with peritoneal carcinomatosis from different primaries has been achieved by performing CRS plus perioperative IPC regimens [7]. After the complete cytoreduction and HIPEC procedure, the present authors administered EPIC procedure to the treatment. HIPEC can be performed by open or closed technique. The authors choose the closed technique because of the advantages including, lack of exposure of operating room staff to the chemotherapeutic agent, minimal heat loss, and no need to the surgeon in the operating room during the procedure [28].

Studies showed that PCI is an important prognostic factor in the survivability of ovarian carcinomatosis [29-32]. The volume of tumor is a major determinant on survivability [30]. The present authors think that complete cytoreduction is crucial on the success of perioperative IPC regimens. Relaparotomy was performed in 28 patients, 16 for stoma closure and second look procedure, and 12 for recurrence. The follow-up period of this study ranged from 15 days to 64 months for all patients; the mean survival time was 22.8 months. Twenty-eight patients (52%) were alive without evidence of the disease. Overall one-year survival was 56%.

Conclusion

In summary, CRS plus HIPEC plus EPIC is a successful option in patients with PC related to gynecological cancers. The authors think that experienced surgical teams can perform CRS with peritonectomy in a reasonable time with an acceptable rate of complications. In order to increase the success of management, maximal surgical resection of metastatic implants should be performed. The authors observed that during second-look exploration, there were extensive adhesions among abdominal wall and organs. This may be related to extensive surgical dissection, peritonectomy, or intra-abdominal administration of paclitaxel. After CRS plus IPC regimens, careful entry into the abdomen and meticulous dissection of abdominal structures are important to reduce surgical complications during repeated abdominal surgeries.

References

[1] Königsrainer I., Horvath P., Struller F., Grischke E.M., Wallwiener D., Königsrainer A., Beckert S.: "Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in recurrent epithelial ovarian cancer with peritoneal metastases: a single centre experience". *Langenbecks Arch. Surg.,* 2014, *399*, 589.

[2] Robella M., Vaira M., Marsanic P., Mellano A., Borsano A., Cinquegrana A., *et al.*: "Treatment of peritoneal carcinomatosis from ovarian cancer by surgical cytoreduction and hyperthermic intraperitoneal chemotherapy (HIPEC)". *Minerva Chir.,* 2014, *69*, 27.

[3] Abu-Zaid A., Azzam A.Z., AlOmar O., Salem H., Amin T., Al-Badawi I.A.: "Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for managing peritoneal carcinomatosis from endometrial carcinoma: a single-center experience of 6 cases". *Ann. Saudi Med.,* 2014, *34*, 159.

[4] Liu Y., Endo Y., Fujita T., Ishibashi H., Nishioka T., Canbay E., Li Y., Ogura S.I., Yonemura Y.: "Cytoreductive surgery under aminolevulinic acid-mediated photodynamic diagnosis plus hyperthermic intraperitoneal chemotherapy in patients with peritoneal carcinomatosis from ovarian cancer and primary peritoneal carcinoma: results of a phase I trial". *Ann. Surg. Oncol.,* 2014, *21,* 4256. doi: 10.1245/s10434-014-3901-5. Epub 2014 Jul 24..

[5] Vizzielli G., Costantini B., Tortorella L., Petrillo M., Fanfani F., Chiantera V., et al.: "Influence of intraperitoneal dissemination assessed by laparoscopy on prognosis of advanced ovarian cancer: an exploratory analysis of a single-institution experience". *Ann. Surg. Oncol.,* 2014, *21*, 3970. doi: 10.1245/s10434-014-3783-6. Epub 2014 May 22.

[6] Sugarbaker P.H.: "Peritonectomy procedures". *Ann. Surg.,* 1995, *221*, 29.

[7] Cavaliere F., Giannarelli D., Valle M., Federici O., Liotta G., Perri P., *et al.*: Peritoneal carcinomatosis from ovarian epithelial primary: combined aggressive treatment". *In Vivo,* 2009, *23*, 441.
[8] Verwaal V.J., Bruin S., Boot H., van Slooten G., van Tinteren H.: "8-year follow-up of randomized trial: cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy in patients with peritoneal carcinomatosis of colorectal cancer". *Ann. Surg. Oncol.,* 2008, *15*, 2426.
[9] Elias D., Lefevre J.H., Chevalier J., Brouquet A., Marchal F., Classe J.M., *et al.*: "Complete cytoreductive surgery plus intraperitoneal chemohyperthermia with oxaliplatin for peritoneal carcinomatosis of colorectal origin". *J. Clin Oncol* 2009, *27*, 681. doi: 10.1200/JCO.2008.19.7160. Epub 2008 Dec 22.
[10] Franko J., Ibrahim Z., Gusani N.J., Holtzman M.P., Bartlett D.L., Zeh H.J. 3rd.: "Cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion versus systemic chemotherapy alone for colorectal peritoneal carcinomatosis". *Cancer,* 2010, *116*, 3756.
[11] Chua T.C., Morris D.L., Saxena A., Esquivel J., Liauw W., Doerfer J., *et al.*: "Influence of modern systemic therapies as adjunct to cytoreduction and perioperative intraperitoneal chemotherapy for patients with colorectal peritoneal carcinomatosis: a multicenter study". *Ann. Surg. Oncol.,* 2011, *18*, 1560.
[12] Sugarbaker P.H.: "Cytoreductive surgery and perioperative intraperitoneal chemotherapy for the treatment of advanced primary and recurrent ovarian cancer". *Curr. Opin. Obstet. Gynecol.,* 2009, *21*, 15.
[13] Sugarbaker P.H.: "Cytoreductive surgery and perioperative intraperitoneal chemotherapy as a curative approach to pseudomyxoma peritonei syndrome". *Eur. J. Surg. Oncol.,* 2001, *27*, 239.
[14] Jayne D.G., Fook S., Loi C.: "Peritoneal carcinomatosis from colorectal cancer". *Br. J. Surg.,* 2002, *89*, 1545.
[15] Glehen O., Osinski D., Cotte E.: "Intraperitoneal chemohyperthermia using a closed abdominal procedure and cytoreductive surgery for the treatment of peritoneal carcinomatosis: morbidity and mortality analysis of 216 consecutive procedures". *Ann. Surg. Oncol*., 2003, *10*, 863.
[16] Stephens A.D., Alderman R., Chang D.: "Morbidity and mortality analysis of 200 treatments with cytoreductive surgery and hyperthermic intraoperative itraperitoneal chemotherapy using the coliseum technique". *Ann. Surg. Oncol.,* 1999, *6*, 790.
[17] Sugarbaker P.H.: "Comprehensive management of peritoneal surface malignancy using cytoreductive surgery and perioperative intraperitoneal chemotherapy: the Washington Cancer Institute approach". *Expert Opin. Pharmacother.,* 2009, *10*, 1965.
[18] Begossi G., Gonzalez-Moreno S., Ortega-Perez G., Fon L.J., Sugarbaker P.H.: "Cytoreduction and intraperitoneal chemotherapy for the management of peritoneal carcinomatosis, sarcomatosis and mesothelioma". *Eur. J. Surg. Oncol*., 2002, *28*, 80.
[19] Feldman A.L., Libutti S.K., Pingpank J.F., Bartlett D.L., Beresnev T.H., Mavroukakis S.M., et al.: "Analysis of factors associated with outcome in patients with malignant peritoneal mesothelioma undergoing surgical debulking and intraperitoneal chemotherapy". *J. Clin. Oncol.,* 2003, *21*, 4560.
[20] Yan T.D., Edwards G., Alderman R., Marquardt C.E., Sugarbaker P.H.: "Morbidity and mortality assessment of cytoreductive surgery and perioperative intraperitoneal chemotherapy for diffuse malignant peritoneal mesothelioma—a prospective study of 70 consecutive cases". *Ann. Surg. Oncol.,* 2007, *14*, 515.
[21] Chua T.C., Yan T.D., Morris D.L.: "Outcomes of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy for peritoneal mesothelioma: the Australian experience". *J. Surg. Oncol.,* 2009, *99*, 109.
[22] Young R.C., Perez C.A., Hoskins W.J.: "Cancer of the ovary". *In:* De Vita V.T., Hellman S., Rosenberg S.A. (eds). *Cancer: principles and practice of oncology*. 4th ed. Philadelphia, Pa: Lippincott-Raven, 1993, 1226.
[23] Glehen O., Osinsky D., Cotte E., Kwiatkowski F., Freyer G., Isaac S., *et al.*: "Intraperitoneal chemohyperthermia using a closed abdominal procedure and cytoreductive surgery for the treatment of peritoneal carcinomatosis: morbidity and mortality analysis of 216 consecutive procedures". *Ann. Surg. Oncol.,* 2003, *10*, 863.
[24] Karadayi K., Turan M., Karadayi S., Alagozlu H., Kilickap S., Buyukcelik A., *et al.*: "Cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy: morbidity and mortality analysis of our patients". *Turkiye klinikleri tip bilimleri dergisi,* 2012, *32*, 162.
[25] Baratti D., Kusamura S., Mingrone E., Balestra M.R., Laterza B., Deraco M.: "Identification of a subgroup of patients at highest risk for complications after surgical cytoreduction and hyperthermic intraperitoneal chemotherapy". *Ann. Surg.,* 2012, *256*, 334.
[26] Karadayi K., Turan M., Sen M.: "A new technique for partial splenectomy with radiofrequency technology". *Surg. Laparosc. Endosc. Percutan. Tech.,* 2011, *21*, 358.
[27] Griffiths C.T.: "Surgical resection of tumor bulk in the primary treatment of ovarian carcinoma". *Natl. Cancer Inst. Monogr.,* 1975, *42*, 101.
[28] Benoit L., Cheynel N., Ortega-Deballon P., Giacomo G.D., Chauffert B., Rat P.: "Closed hyperthermic intraperitoneal chemotherapy with open abdomen: a novel technique to reduce exposure of the surgical team to chemotherapy drugs". *Ann. Surg. Oncol.,* 2008, *15*, 542.
[29] Plaisant N., Quenet F., Fabbro M., Gourgou S., Gutowski M., Saint Aubert B., Rouanet P.: "Secondary debulking surgery and intraperitoneal chemotherapy in advanced or recurrent epithelial ovarian cancer". *Gynecol. Obstet. Fertil.,* 2004, *32*, 391.
[30] Piso P., Dahlke M.H., Loss M., Schlitt H.J.: "Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy in peritoneal carcinomatosis from ovarian cancer". *World. J. Surg. Oncol.,* 2004, *2*, 21.
[31] Ryu K.S., Kim J.H., Ko H.S., Kim J.W., Ahn W.S., Park Y.G., *et al.*: "Effects of intraperitoneal hyperthermic chemotherapy in ovarian cancer". *Gynecol. Oncol.,* 2004, *94*, 325.
[32] Rufián S., Muñoz-Casares F.C., Briceño J., Díaz C.J., Rubio M.J., Ortega R., *et al.*: "Radical surgery, peritonectomy and intraoperative intraperitonealchemotherapy for the treatment of peritoneal carcinomatosis in recurrent or primary ovarian cancer". *J. Surg. Oncol.,* 2006, *94*, 316.

Address reprint requests to:
S. KARAKUS, M.D.
Department of Obstetrics and Gynecology
Cumhuriyet University Faculty of Medicine
Kayseri Street
58140 Sivas, Turkey
e-mail: karakussavas@yahoo.com