

Salvage Surgery Due To Bowel Obstruction in Advanced or Relapsed Ovarian Cancer Resulting in Short Bowel Syndrome and Long-Life Total Parenteral Nutrition

Surgical and Clinical Outcome

Christina Fotopoulou, PhD, MD,*† Elena Ioana Braicu, MD,* Sara-Lea Kwee, MD,*
 Marc Kuhberg, MD,* Rolf Richter, MD, PhD,* Klaus Pietzner, MD,* Aarne Feldheiser, MD,‡
 Marcus Bahra, MD,§ Sven Christian Schmidt, MD, PhD,§ and Jalid Sehouli, PhD, MD*

Objective: Salvage surgery for patients with highly advanced or relapsed epithelial ovarian cancer (EOC) complicated by bowel obstruction and resulting in short bowel syndrome (SBS) constitutes a therapeutic dilemma. Our aim was to evaluate surgical and clinical outcome in these highly palliative situations.

Methods: We evaluated all patients with EOC who underwent salvage extraperitoneal en bloc intestinal resection with terminal ileostomy or jejunostomy resulting in SBS and total parenteral nutrition owing to bowel obstruction between May 2003 and January 2012 in our institution.

Results: Thirty-seven patients were identified (median age, 58 years; range, 22–71 years), 3 (8.1%) with primary and 34 (91.6%) with relapsed EOC. Five patients (13.5%) were platinum sensitive. Median residual intestinal length was 70 cm (range, 10–180 cm); 21 patients (56.8%) had a residual intestinal length less than 1 m. Operative 30-day mortality and major morbidity rates were 10% and 51%, respectively. Median overall survival was 5.6 months (range, 0.1–49 months). One-year and 2-year overall survival rates were 18.3% (95% confidence interval, 5.1%–31.5%) and 8.1% (95% confidence interval, 0%–18.0%), respectively. Within a median follow-up period of 5 months (range, 0.2–49 months), 4 patients (10.8%) are still alive. No significant differences in survival were seen between patients with or without major complications, tumor residuals, or residual intestinal length of less than 1 m versus greater than 1 m.

Conclusions: Salvage palliative surgery in EOC due to bowel obstruction resulting in SBS and in need of long-life total parenteral nutrition is associated with high morbidity rates and low overall survival. These surgeries should ideally be performed only in a multidisciplinary setting with adequate infrastructure and possibility of home care support. Conservative management should be the route of action in the absence of acute abdomen or intestinal perforation.

Key Words: Ovarian cancer, Tumor debulking, Bowel obstruction, Morbidity, Survival, Short bowel syndrome

Received December 27, 2012, and in revised form May 26, 2013.

Accepted for publication June 7, 2013.

(*Int J Gynecol Cancer* 2013;23: 1495–1500)

*Department of Gynecology, European Competence Center for Ovarian Cancer, Charité, Campus Virchow Clinic, University Hospital, Berlin, Germany; †Ovarian Cancer Action Research Centre, Department of Surgery and Cancer, Imperial College London, London United Kingdom; ‡Department of Anaesthesiology and Intensive Care Medicine, Charité, Universitaetsmedizin Berlin, Campus Virchow-
 Copyright © 2013 by IGCS and ESGO
 ISSN: 1048-891X

DOI: 10.1097/IGC.0b013e31829f81ca

Klinikum and Campus Charité Mitte; and §Department of General, Visceral and Transplantation Surgery, Charité, Campus Virchow Clinic, University Hospital, Berlin, Germany.

Address correspondence and reprint requests to Jalid Sehouli, MD, PhD, Department of Gynecology, European Competence Center for Ovarian Cancer, Charité, Campus Virchow Clinic, University Hospital, Augustenburger Platz 1, 13353 Berlin, Germany.
 E-mail: sehouli@aol.com.

The authors declare no conflicts of interest.

The surgical management of epithelial ovarian cancer (EOC) is undergoing an era of increased radicality with incorporation of multivisceral techniques aiming at “optimal” tumor residuals and thus most favorable outcome.^{1–6} Attributed to the diffuse tumor dissemination pattern along the peritoneal layers,⁷ patients with EOC often present with the clinical picture of impaired intestinal passage and eventually bowel obstruction in the advanced primary and in relapsed EOC. The newly emerging novel implementation of targeted therapies with antiangiogenic potential may additionally favor fistula formation or intestinal perforation.^{8,9} Massive systemic and surgical pretreatment and extensive tumor dissemination, combined with acute systemic inflammatory immunologic response, make any surgical intervention in this setting highly challenging, while potentially associated with high morbidity and mortality rates. Appropriate balancing of risks and benefits is required to design the optimal treatment options tailored around the individual needs. The patient communication processes are currently based on rather scattered monocentric data series because data from large multicenter analyses are broadly lacking.

Surgical interventions include various surgical techniques and strategies, such as en bloc resections of the involved intestinal package and terminal proximal ileostomy or jejunostomy, because owing to the severe peritoneal carcinosis and inflammation, no plane dissection with anastomotic and repair techniques are feasible. Short bowel syndrome (SBS) with subsequent total parenteral nutrition (TPN) is therefore in some cases inevitable.⁸

Data evaluating surgical and clinical outcome after such salvage procedures in advanced EOC are scarce. The aim of the present analysis was to systematically assess the surgical morbidity, overall outcome, and quality of life—where available—after emergency laparotomy due to bowel obstruction in primary advanced or relapsed EOC, which resulted in SBS and long-life TPN.

MATERIALS AND METHODS

We conducted a retrospective evaluation of all primary or relapsed patients with EOC who underwent salvage extraperitoneal en bloc intestinal resection with terminal ileostomy or jejunostomy resulting in SBS and whole-life TPN due to bowel obstruction between May 2003 and January 2012 in the Department of Gynecology at the Charité, Campus Virchow Clinic. The cases of bowel perforation or fistula were excluded to avoid inhomogeneous results. All our evaluated patients had a functional or anatomic SBS, by bowel meaning small bowel. We however performed a subanalysis of patients with residual intestinal length of less than 1 m, as an additional surrogate marker of extensive surgery and severity of symptoms.

In case of chronic subileus/ileus, affected patients were always initially treated in a conservative fashion with nasogastric tube, antibiotics, intravenous substances inducing the intestinal propulsive activity such as metoclopramide and neostigmin, food abstention, and corticosteroids. Only in failure of conservative treatment and in the development of an acute abdomen or radiographic or endoscopic findings of a

complete stop in the ileum or large intestine was surgery indicated. In case of upper gastrointestinal obstruction such as gastric outlet narrowing, endoscopic stent placement was the first treatment of choice.

All operations were performed by 1 of 4 gynecologic oncologic surgeons in an interdisciplinary team approach with specialized general surgeons, anesthesiologists, and intensive care practitioners.

The total number of patients operated on at the same time owing to EOC of any stage was 643 (primary, 310; relapsed, 333). Staging was defined in accordance with International Federation of Gynecology and Obstetrics (FIGO) criteria for ovarian epithelial carcinoma.¹⁰

All procedures were performed per midline laparotomy. Due to severe adhesions, peritonitis, and peritoneal carcinosis, an extrafascial dissection was performed after careful exposure and dissection of the ureters, pelvic vessels axis, aorta, inferior vena cava and duodenum. The whole intestinal package was en bloc dissected and followed up to the first intestinal loop from the ligament of Treitz that was clear of severe lesions and free of passage. This was then diverted as a terminal ileostomy or jejunostomy. In case of tumor and peritonitis involvement of additional structures such as the gall bladder, the spleen, or the urinary bladder, then the adjacent organs were also removed in the en bloc resection specimen. All patients were operated on via an extraperitoneal approach not with the intention of cytoreduction but for a simpler dissection of the organs, aiming hence to reduce the additional injury of adjacent intestinal loops and other organs. Owing to the peritonitis and/or the previous surgeries, the adhesions and the intraperitoneal circumstances were so severe that any primarily intraperitoneal approach would additionally aggravate any surgical effort and prolong surgical time and risk of injury.

To avoid anastomotic insufficiency and secondary wound healing problems in this acute situation with dilated bowel walls, number of intestinal anastomoses were tried to be kept limited—maximal 2—or even not at all performed. At the end of the procedure, the remaining small intestine was meticulously measured from the ligament of Treitz to the terminal stoma.

In every patient, the detailed tumor pattern was intraoperatively assessed by an independent person based on the surgical procedures performed and by a systematic interview of the surgical team. Postoperatively, all histological findings and collected data were entered into a validated documentation system (“Intraoperative Mapping of Ovarian Cancer”[IMO]), especially developed for ovarian neoplasms with special focus on the description of the tumor pattern, maximal tumor burden, postoperative tumor residuals (0, <0.5, <1, <2, and >2 cm),¹¹ and the amount of preoperative ascites (none, <50 mL, or >500 mL).

All additional patients’ data including history as well as follow-up and survival data were abstracted from the patients’ records. Survival data of the patients were last updated on March 2012 based on patient’s files and/or responses from their physicians or insurance companies.

All patients received postoperatively a nutritional therapy in terms of a TPN enriched with vitamins and minerals such as vitamins A, D, E, K, and B12, calcium, magnesium, iron, folic acid, and zinc via central catheter and a

TABLE 1. Characteristics of Patients With EOC Who Underwent Salvage Surgery for Advanced Disease Resulting in SBS (n = 44)

Characteristics	Median (Range)
Age, y	58 (22–71)
CA-125 before surgery, U/mL	357 (32–2324)
Time after primary diagnosis, mo	26 (0–173)
No. tumor relapses before salvage surgery	2 (0–5)
	Patients, n (%)
Tumor status	
Primary	3 (8.1)
Relapsed	34 (91.6)
Platinum sensitive	5 (13.5)
Ascites	
None	17 (45.9)
<500 mL	12 (32.4)
>500 mL	7 (18.9)
Histology	
Serous papillary	29 (78.4)
Mucinous	3 (8.1)
Endometrioid	2 (5.4)
Clear cell	1 (2.7)
Differentiation grade	
Grade 1	2 (5.4)
Grade 2	11 (29.7)
Grade 3	19 (51.4)

subsequently venous port by a special “short bowel syndrome” team including special measurement tests of malnutrition signs, bioimpedance analysis, and calorimetry. According to the performance status of the patients, they were postoperatively offered a systemic chemotherapy or merely additional support in terms of a palliative care at home with a “home care” physician team or a hospice or a palliative care unit within our institution or within our cancer network.

Intraoperative Mapping of Ovarian Cancer

“IMO” represents a detailed and objective surgical and histopathological documentation system developed and validated to obtain a better and more objective description of the ovarian tumor spread within the abdominal cavity and to define more precisely the histopathological features of the malignancy.^{3,11} Three “IMO levels” divide the abdomen into 3 spaces as follows: lower (level 1), middle (level 2), and upper (level 3) abdomen. Nine “IMO fields,” 3 at each level, provide a subclassification of the peritoneal cavity aiming at a more precise documentation of the tumor dissemination pattern. The patients’ informed consent was always given before surgery as well as sample collection and documentation.

Follow-up

Patients were regularly evaluated at the end of the treatment for evidence of disease recurrence. Clinical examinations, transvaginal and transabdominal ultrasound, CA-125 (where applicable) assays were performed every 3 months. A computed tomography/magnetic resonance imaging scan was ordered if the previously mentioned examinations revealed any pathology.

Statistics

All data are presented as frequency and rate for categorical variables or median and range for continuous variables. Comparisons between patients surviving less than 6 months and patients surviving at least 6 months were performed using Fisher exact test, χ^2 test, Kendall τ b or Mann-Whitney U test where appropriate. Estimates of median survival and 1-year and 2-year survival rates were calculated using the Kaplan-Meier method. Log-rank tests were used for univariate statistical comparisons. All data were analyzed using IBM SPSS Statistics 19.0 (SPSS Inc, Chicago, Ill), and $P < 0.05$ was considered statistically significant.

RESULTS

We evaluated 37 consecutive patients (median age, 58 years; range, 22–71 years) who underwent salvage emergency surgery during a 9-year evaluation period. Most patients (91.6%) were in the relapsed setting of the disease, whereas 8.1% presented with an acute abdomen at the onset of the disease. Median number of previous operations was 3 (range, 0–6). Patient- and cancer-related characteristics are presented in detail in Table 1.

Within a median follow-up time of 5 months (range, 0.2–49 months), 40 patients (89.2%) died. Median overall survival (OS) was 5.6 months (range, 0.1–49 months). One-year and 2-year OS rates were 18.3% (95% confidence interval [CI], 5.1%–31.5%) and 8.1% (95% CI, 0%–18.0%), respectively. The 2 long survivors have lived 26 and 49 months since the salvage operation.

Overall, 15 patients (40.5%) lived 6 months or longer. When comparing the 2 subgroups of patients who survived more than 6 months versus the patients who survived less than 6 months, no significant difference could be noted regarding median age, residual small intestine length, preoperative CA-125 values, grading, histological subtype, amount of ascites, lymph node involvement, postoperative residual tumor disease, platinum sensitivity status, presence of peritoneal carcinosis, and tumor dissemination pattern as assessed by IMO. However, a significant correlation with a longer (>6 months) survival was identified with lower initial FIGO stage ($P = 0.011$). None of the patients who survived longer than 6 months had an initial FIGO stage IV.

The surgery included a multivisceral resection approach with a median duration of 270 minutes (range, 148–596 minutes). Surgery-related characteristics are presented in Table 2. Median length of hospital stay was 24 days (range, 10–76 days). In 5 patients (13.5%), postoperative tumor residuals were smaller than 0.5 cm in terms of a diffuse small nodule peritoneal

TABLE 2. Data of Perioperative Management, Operative Mortality and Morbidity (n = 44)

	Median (Range)
Operation time, min	270 (148–596)
Transfusion of erythrocyte concentrates, U	2 (0–12)
Length of stay in intensive care unit, d	2.5 (0–31)
Length of hospital stay, d	24 (10–76)
Intestinal length	70 cm (10–180)
<1 m	21 (56.8%)
>1 m	16 (43.2%)
	Patients, n (%)
Postoperative tumor residuals	
None	5 (13.5)
<0.5 cm	5 (13.5)
0.5–1 cm	6 (16.2)
1–2 cm	3 (8.1)
>2 cm	15 (40.5)
Procedures performed	
Hysterectomy	4 (10.8)
Salpingoovarectomy	3 (8.1)
Omentectomy	6 (16.2)
Pelvic lymph node dissection	4 (10.8)
Para-aortic lymph node dissection	5 (13.5)
Appendectomy	5 (13.5)
Liver capsule resection	0 (0)
Cholecystectomy	1 (2.7)
Splenectomy	2 (5.4)
Partial bladder resection	1 (2.7)
Ureteral resection	0 (0)
Any major complications	19 (51)
Sepsis	1
Pulmonary embolism	2
Peritonitis	4
Pleura effusion	3
Relaparotomy	12
Anastomotic insufficiency	5
Abscess, secondary wound healing	1
Postoperative bleeding	2
Intestinal perforation	1
Rupture of abdominal wall closure	1
Peritonitis	1
Minor postoperative procedures (drainage, abscess dissection)	7 (18.9) (Several complications are possible in the same patient).
Adjuvant treatment	
None	13 (35.1)
Platinum based	12 (34.3)

dissemination. No significant differences in OS could be noted between patients with tumor residuals less than 0.5 cm versus patients with tumor residuals greater than 0.5 cm ($P = 0.61$).

In 21 patients (56.8%), the surgery ended in a residual small bowel of less than 100 cm. When evaluating OS according to the residual intestinal length, then median OS for those patients with less than 1-m residual small bowel was 4.7 months (95% CI, 2.4–6.9) versus 7.0 months (95% CI, 2.2–12.0) for those with a residual length of more than 100 cm and hence showing a clear trend toward better survival, although not reaching statistical significance ($P = 0.65$).

Fifty-one percent of the patients (n = 19) developed a major postoperative complication. Twelve patients (32.4%) underwent a relaparotomy mainly owing to peritonitis and/or anastomotic insufficiency. Data are also presented in Table 2. A cross table correlation of major morbidity and length of residual intestine did not reveal any statistically significant subgroups (Table 3).

Furthermore, when classifying OS according to the incidence of major morbidity, no significant differences were noted between the patients with versus without any major complication ($P = 0.739$).

Eight patients (21.6%) were not able to receive any postoperative antitumor treatment such as systemic chemotherapy, whereas in 8 patients (21.6%), carboplatin was applied. There was a significant difference in median survival in favor of those patients who received any chemotherapy versus those who did not (5.9 months vs 2.6 months, $P = 0.007$); however, this could imply a significant bias because the patients who died early or were too weak for chemotherapy had anyway a worse prognosis.

Assessment of the quality of life of the 4 patients alive using the SF-12 Health Survey validated questionnaire revealed significantly lower physical and mental patient scores compared with those of the general healthy population. Values are presented in Table 4.

Of the 33 patients who died, 20 (60%) did so in a hospital or a hospice, whereas the other 13 (45%) died at home.

DISCUSSION

The present analysis is the first to systematically analyze the surgical and clinical outcome of salvage surgery in advanced primary and recurrent EOC due to not conservatively manageable bowel obstruction resulting in postoperative SBS and long-life TPN. We could show that in this stage of the disease, usual prognosticators of survival such as platinum resistance status, tumor residuals, histological subtype, and lymph node involvement have no impact on overall outcome. The only significant parameter identified to have a significant impact on survival was the initial FIGO stage; none of the FIGO IV patients lived longer than the median survival time of 6 months. We could furthermore show that such salvage procedures are associated with high morbidity and mortality rates; however, in some selected cases, they may even prolong survival for a substantial amount of time and thus successfully overcome the acute life-threatening incidents.

Epithelial ovarian cancer seems to behave differently from other epithelial cancer types because its constant, almost

TABLE 3. Cross Table Regarding the Correlation of Major Morbidity and Length of Residual Intestine in the 44 Patients With EOC Who Underwent Salvage Surgery

			Intestinal Length		Total	
			<1 m	>1 m		
Major complication	Yes	Patients, n	10	6	16	<i>P</i> = 0.74
		%	47.6	37.5	43.2	
	No	Patients, n	11	10	21	
		%	52.4	62.5	56.8%	
Total		Patients, n	25	21	16	
		%	100.0	100.0	100.0	

pathognomonic feature is its local and lymphatic dissemination to the peritoneal and pleural layers by a paucity of visceral distant metastases via hematogenous pathways. Locoregional peritoneal disease is what most patients die of, in terms of bowel obstruction, cachexia, hypoproteinemia from ascites, organ failure, and exhaustion.⁷ The unusual behavior and natural history of EOC has therefore generated unique therapeutic strategies that recognize the important contribution of locoregional control to survival for this disease.

In cases of acute intestinal complications such as bowel obstruction, the choice of the adequate therapeutic pathway is highly challenging. The cancer-induced tissue alterations and the overall low patients reserve constitute a major challenge for both the patients themselves and the treating physicians, so that often, such acute situations provoke a therapeutic nihilism and overall hesitation of active surgical measures. In previous analyses of our center, we could indeed show that patients operated on in acute situations had significantly higher rates of anastomotic insufficiency compared with those operated within a planned setting,⁸ as we also saw that the rate of anastomotic insufficiency seems to be higher at primary debulking with tumor residuals compared with those without.¹² For these reasons, although no randomized trials exist to prove the safety of a primary anastomosis in an acute setting with peritonitis, the high probability of an intestinal stoma should be preoperatively discussed with the affected patients.

Epithelial ovarian cancer rarely develops through visceral metastases; organ involvement is mainly due to direct extension by continuous tumor growth of the visceral peritoneum. Tumor dissemination patterns in epithelial ovarian cancer usually respect the peritoneal borders, therefore tumor resection is best achieved by an extraperitoneal approach of the tumor mass and en bloc dissection of all the tumor

involved organs together with the adjacent peritoneum, after their dissections from the ureteric and blood vessel level in the lower abdomen as well as the duodenum, pancreas, and biliary duct in the upper abdomen. Extensive multivisceral techniques are increasingly being included in the surgical armamentarium of advanced disease management.^{5,13,14} This reflects also the optimal approach in acute situations. A simple local intestinal resection with reanastomosis or barrel loop ileostomy is often not feasible because the combination of peritoneal carcinosis and peritonitis makes a dissection in the physiological planes impossible and of high risk of further injury.⁸

The mortality and morbidity rates reported here are equivalent to similar situations in gastrointestinal tumors¹⁵ but less compared with the planned secondary and tertiary cytoreduction for EOC.^{16,17}

Highly interesting is the fact that although increasing evidence indicates that even in advanced stages of the EOC, disease such as the tertiary cytoreduction the factor “tumor residuals” retains its highly significant impact on survival, this loses any significance at salvage surgery owing to intestinal complications.^{16,17} This may be mainly attributed not only to the fact that in these acute and even life-threatening situations, other factors such as immunological acute phase reactions resume the major role¹⁰ but also to the fact that the goal of surgery in this setting is not the cytoreduction per se but the restoration of intestinal passage. Moreover, it is well established that in relapsed EOC, patients do not benefit from surgery with “optimal residuals” but only from a complete macroscopic resection.^{11,18} Because, in our patients as a collective, the vast majority were in the relapsed situation, optimal tumor residuals of 0.5 cm were of no beneficial prognostic significance compared with gross residual disease.

TABLE 4. Assessment of the Quality of Life of the 4 Alive Patients With EOC Who Underwent Salvage Surgery Resulting in SBS According to the SF-12 Health Survey Validated Questionnaire

	Patients With EOC	Healthy Population	<i>P</i>
SF-12 physical score, mean (SD)	36.68 (2.2)	50 (10)	0.009
SF-12 psychological score, mean (SD)	21.36 (6.5)	50 (10)	0.017

The physical and mental scores of the patients were significantly lower than the scores of the general healthy population.

The clear trend of better survival when residual small bowel length was more than 1 m underlines the fact that surgical effort should also be focused on preserving as much small bowel as possible. The nonsignificant difference might be attributed to the overall small number of cases in this cohort analysis.

A major issue is the highly crucial role of a psychosocial and nutritional support network to provide TPN at home. A large number of patients had the chance to be provided with a strict TPN program and die at home, which did not imply hospital care. Therefore, multidisciplinary teams consisting of nutritional specialists, dieticians, gastroenterologists, and psychooncologists are indispensable for the successful outcome of such surgeries.

To conclude, we showed that salvage palliative surgery in EOC due to bowel obstruction resulting in SBS and in need of long-life TPN is associated with high morbidity rates and low overall prognosis; therefore, conservative management incorporating endoscopic approaches should be the route of action in the absence of acute abdomen or intestinal perforation. Careful patient selection, thorough discussion with the patients about the risks and benefits, and, more importantly, a solid network to support TPN at home are indispensable to perform such salvage radical procedures. Multidisciplinary setting, adequate infrastructure, and the possibility of home care support are indispensable.

REFERENCES

1. Chang SJ, Bristow RE. Evolution of surgical treatment paradigms for advanced-stage ovarian cancer: redefining 'optimal' residual disease. *Gynecol Oncol.* 2012;125:483–492.
2. Chi DS, Bristow RE, Armstrong DK, et al. Is the easier way ever the better way? *J Clin Oncol.* 2011;29:4073–4075.
3. Bristow RE. Surgical standards in the management of ovarian cancer. *Curr Opin Oncol.* 2000;12:474–480.
4. du Bois A, Quinn M, Thigpen T, et al. 2004 consensus statements on the management of ovarian cancer: final document of the 3rd International Gynecologic Cancer Intergroup Ovarian Cancer Consensus Conference (GCIIG OCCC 2004). *Ann Oncol.* 2005;16:viii7–viii12.
5. Chi DS, Franklin CC, Levine DA, et al. Improved optimal cytoreduction rates for stages IIIC and IV epithelial ovarian, fallopian tube, and primary peritoneal cancer: a change in surgical approach. *Gynecol Oncol.* 2004;94:650–654.
6. du Bois A, Reuss A, Pujade-Lauraine E, et al. Role of surgical outcome as prognostic factor in advanced epithelial ovarian cancer: a combined exploratory analysis of 3 prospectively randomized phase 3 multicenter trials: by the Arbeitsgemeinschaft Gynaekologische Onkologie Studiengruppe Ovarialkarzinom (AGO-OVAR) and the Groupe d'Investigateurs Nationaux Pour les Etudes des Cancers de l'Ovaire (GINECO). *Cancer.* 2009;115:1234–1244.
7. Janczar S, Graham JS, Paige AJW, et al. Targeting locoregional peritoneal dissemination in ovarian cancer. *Expert Rev Obstet Gynecol.* 2009;4:133–147.
8. Sehouli J, Papanikolaou G, Braicu EI, et al. Feasibility of surgery after systemic treatment with the humanized recombinant antibody bevacizumab in heavily pretreated patients with advanced epithelial ovarian cancer. *Ann Surg Oncol.* 2012;19:1326–1333.
9. Burger RA. Overview of anti-angiogenic agents in development for ovarian cancer. *Gynecol Oncol.* 2011;121:230–238.
10. Shimizu T, Hanasawa K, Sato K, et al. Direct hemoperfusion with polymyxin-B-immobilized fiber columns improves septic hypotension and reduces inflammatory mediators in septic patients with colorectal perforation. *Langenbecks Arch Surg.* 394:303–311.
11. Harter P, du Bois A, Hahmann M, et al. Surgery in recurrent ovarian cancer: the Arbeitsgemeinschaft Gynaekologische Onkologie (AGO) DESKTOP OVAR trial. *Ann Surg Oncol.* 2006;13:1702–1710.
12. Fotopoulou C, Richter R, Braicu EI, et al. Can complete tumor resection be predicted in advanced primary epithelial ovarian cancer? A systematic evaluation of 360 consecutive patients. *Eur J Surg Oncol.* 2010;36:1202–1210.
13. Zivanovic O, Eisenhauer EL, Zhou Q, et al. The impact of bulky upper abdominal disease cephalad to the greater omentum on surgical outcome for stage IIIC epithelial ovarian, fallopian tube, and primary peritoneal cancer. *Gynecol Oncol.* 2008;108:287–292.
14. Chi DS, Zivanovic O, Levinson KL, et al. The incidence of major complications after the performance of extensive upper abdominal surgical procedures during primary cytoreduction of advanced ovarian, tubal, and peritoneal carcinomas. *Gynecol Oncol.* 2010;119:38–42.
15. Yeo ES, Ng KH, Eu KW. Perforated colorectal cancer: an important differential diagnosis in all presumed diverticular abscesses. *Ann Acad Med Singapore.* 2011;40:375–378.
16. Fotopoulou C, Richter R, Braicu IE, et al. Clinical outcome of tertiary surgical cytoreduction in patients with recurrent epithelial ovarian cancer. *Ann Surg Oncol.* 2011;18:49–57.
17. Sehouli J, Richter R, Braicu EI, et al. Role of secondary cytoreductive surgery in ovarian cancer relapse: who will benefit? A systematic analysis of 240 consecutive patients. *J Surg Oncol.* 2010;102:656–662.
18. Harter P, Hahmann M, Lueck HJ, et al. Surgery for recurrent ovarian cancer: role of peritoneal carcinomatosis: exploratory analysis of the DESKTOP I Trial about risk factors, surgical implications, and prognostic value of peritoneal carcinomatosis. *Ann Surg Oncol.* 2009;16:1324–1330.

