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# Patient Selection for Ovarian Cancer Debulking Surgery

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Janos Balega

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<http://dx.doi.org/10.5772/intechopen.71585>

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## Abstract

Complete surgical cytoreduction is the most important adverse prognostic factor for survival in ovarian cancer. To achieve this, surgeons often have to perform radical and ultraradical procedures with associated significant postoperative morbidity and mortality. Adverse events are most pronounced in patients with borderline or suboptimal capacity to withstand the stress related to surgery. In frail, elderly, malnourished patients, surgeons face limitations to exercise maximum surgical effort; therefore, alternative treatment strategies are required. Neoadjuvant chemotherapy offers a safe and effective way to enhance recovery after delayed debulking surgery in patients who are not optimal candidates for primary debulking surgery.

**Keywords:** debulking surgery, ovarian cancer, neoadjuvant chemotherapy, nutrition, age

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## 1. Introduction

Primary debulking or cytoreductive surgery followed by adjuvant chemotherapy has long been the mainstay of treatment for patients with advanced ovarian cancer. The goal of surgery is complete cytoreduction with no visible residual cancer as it is associated with better survival compared with residuals 0–1 cm or >1 cm [1–6]. During the past two decades, new surgical techniques were incorporated into the armamentarium of gynecologic oncologists to address disease located in the upper abdomen. Such paradigm shift in surgical philosophy has resulted in higher rate of complete cytoreduction, and this has translated into survival benefit [7]. Upper abdominal resection (the so-called ultraradical debulking) should only be performed if complete cytoreduction is achievable as even the presence of minimal residual disease will adversely affect the survival of patients [8].

For long, upfront surgery had been the standard approach for patients with advanced ovarian cancer; however, a new treatment strategy using neoadjuvant chemotherapy followed by delayed primary surgery has emerged two decades ago and been supported by retrospective

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studies [9–11]. However, Bristow et al. in their meta-analysis demonstrated inferior outcomes for patients undergoing neoadjuvant chemotherapy, although this analysis was heavily biased by the retrospective nature of the studies included [12].

In 2010, Vergote et al. published a prospective, randomized, multi-institutional study on neoadjuvant chemotherapy followed by delayed primary surgery vs. upfront surgery followed by adjuvant chemotherapy. Although the study was heavily criticized by proponents of upfront surgery, it supported a new treatment paradigm by demonstrating equivalent survival with significantly reduced morbidity and mortality for patients undergoing neoadjuvant chemotherapy followed by delayed primary surgery [2]. Kehoe et al. in their prospective, randomized CHORUS trial corroborated these findings [4].

Since the publication of these trials, professional debate has been going on whether to offer primary surgery or neoadjuvant chemotherapy for patients with advanced ovarian cancer and what is the appropriate rate of upfront surgery in cancer centers [13–15]. There has been an apparent dichotomy between highly specialized, quaternary referral centers and smaller units with lower surgical volume and less generous resources. Unfortunately, most cancer centers fail to publish their denominator data, i.e., their referral pathways, the background ovarian cancer population of their catchment area, and the percentage of patients not taken to theater or not receiving any treatment, which brings a significant selection bias into these publications and scientific debates. This makes both the interpretation of the published data and their extrapolation to day-to-day practice difficult [16].

Both EORTC55971 and CHORUS trials have received extensive criticism. Indeed, significant recruitment bias was observed in both studies: patients with large tumor load, unresectable disease, and poor performance status were overrepresented in these studies, and, therefore, many clinicians have been reluctant to extrapolate the results into clinical practice. Furthermore, the rate of complete/optimal resection in these studies was low; in the EORTC55971 trial, <1 cm residual cancer was achieved in only 41.6% of the patients in the upfront surgery arm. Although it improved to 80.7% in the neoadjuvant chemotherapy arm, this surprisingly did not translate into survival benefit [2]. The CHORUS trial reported similar results at 41 and 73%, with no therapeutic advantage associated with such increase [4].

In view of this criticism, the survival results of two subsequent randomized trials, the SCORPION study from Italy and the JCOG0602 study from Japan, are highly awaited [17, 18]. Both studies confirmed significantly reduced morbidity and mortality associated with delayed primary surgery following neoadjuvant chemotherapy compared with upfront debulking surgery. In the Italian study, 91 and 90.4% of the patients with large-volume stage 3C and 4 ovarian cancer had <1 cm residual disease after surgery, in the upfront surgery and neoadjuvant chemotherapy arms, respectively. In the upfront surgery arm, 53% of the patients developed major postoperative complications compared with 6% of the neoadjuvant chemotherapy arm.

In the Japanese trial, 37% of the patients with primary debulking achieved residual disease <1 cm and 82% of those undergoing delayed surgery after neoadjuvant chemotherapy. Interestingly, one-third of the patients in the upfront surgery arm received an interval debulking

surgery, bearing in mind that the use of preoperative laparoscopy to select out unresectable cases was not permitted in the study protocol. Severe complications developed in 5% of the patients in the neoadjuvant chemotherapy arm vs. 15% of the patients in the upfront surgery arm. Survival data for both studies are awaited to confirm superiority of neoadjuvant chemotherapy for the patient cohorts represented in the study.

Despite all criticism, clinical uptake of neoadjuvant chemotherapy has increased worldwide; in the USA, it has increased from 9% in 2003 to 23% in 2013 [19]. Recently, in their joint clinical practice guideline, the Society of Gynecologic Oncology and the American Society of Clinical Oncology have promoted a more selective approach for patients with advanced ovarian cancer, recommending upfront surgery or neoadjuvant chemotherapy for patients with different clinical characteristics [20, 21].

In clinical practice, upfront surgery and neoadjuvant chemotherapy are not equivalent alternatives for all patients. The aim of this review is to aid the readers to find the most appropriate way to treat their patients by analyzing the factors affecting clinical outcome in ovarian cancer.

## 2. Selecting the right patient for the right treatment

There are numerous clinicopathological factors influencing the outcome of ovarian cancer patients:

- **Patient-related factors:** age, performance status, comorbidities, nutritional status
- **Cancer-related factors:** grade, stage, tumor extent and size, platinum resistance, molecular subtype
- **Treatment-related factors:** residual cancer after surgery, time from surgery to chemotherapy, complications during treatment
- **Institutional factors:** surgical philosophy and skills, available resources, availability of multidisciplinary team

### 2.1. Age

Age is an independent prognostic factor for survival for patients with advanced ovarian cancer, but age itself also has an impact on patients' ability to cope with stress related to major surgical interventions [22]. The reserves of the cardiovascular, renal, pulmonary, central nervous, and skeletomuscular systems progressively decline in the elderly, and their physiological response to stress is different. Due to altered physiology of the elderly, the pharmacokinetics and pharmacodynamics of medications especially anesthetics are altered.

Mahdi et al. in their review of postoperative outcome of ovarian cancer patients found that patients older than 70 but particularly those over 80 years of age more frequently developed chronic kidney failure, cardiorespiratory diseases, and neurological deficit [23]. Compared with patients <60 years of age, the odds ratio for 30-day mortality after surgery was 3.7, 3.1, and 9.3, for patient aged 60–69, 70–79, and ≥80, respectively. While 1% of the patients younger

than 60 died after operation, 9% of the over 80s suffered fatal complications postoperatively. There was no significant difference in the mortality of patients younger or older than 70 years who received neoadjuvant chemotherapy and underwent delayed primary surgery. Similarly, patients younger than 60 developed less postoperative complications than those aged 60–69, 70–79, and  $\geq 80$  (25% vs. 34%, 35%, and 39%, respectively).

Although old age alone is not a contraindication for debulking surgery, but it is an important surrogate to take into account when planning treatment for advanced ovarian cancer. Patients over 80 years with extensive disease requiring four-quadrant resection may benefit from alternative treatment approach, such as neoadjuvant chemotherapy with delayed debulking surgery or, if frail with multiple comorbidities, primary chemotherapy with no surgical intervention.

## 2.2. Nutritional status

Poor nutritional status has long been demonstrated to be an adverse prognostic factor for postoperative complications, due to reduced immunity and impaired repair capacity [24–28]. Cancer-related hypoalbuminemia is a multifactorial condition related to reduced protein intake, cancer-related systemic inflammation, and muscle protein depletion and is a marker for malnutrition [29]. Patients with advanced ovarian cancer often present with ascites, and in two-thirds of the patients, it is associated with cachexia, loss of muscle weight, and hypoproteinemia-hypoalbuminemia [30].

It has been demonstrated that ovarian cancer patients with hypoalbuminemia (defined as the serum albumin level less than 35 g/L) were 5–10 times more likely to develop severe complications after debulking surgery than those with a normal albumin level. The mortality rates for patients with a low and normal serum albumin level are 12 and 2.5%, respectively [22, 23, 31, 32]. Ovarian cancer patients with a low serum albumin level have a significantly higher anastomotic leakage rate than those with normal levels (18–21% vs. 0–3.4%), and the rate of wound-related complications, infections, and septicemia is also significantly higher [33, 34].

Global clinical assessment of ovarian cancer patients is paramount in diagnosing malnutrition; a single measurement of BMI is unreliable due to excess weight associated with ascites and generalized edema. A low serum albumin level is associated with malnutrition and is an easy test prior to surgery; it is a strong predictor for postoperative morbidity. As two-thirds of ovarian cancer patients are malnourished, it is important to explore the ways to improve nutrition and albumin levels prior to cytoreductive surgery.

Total parenteral nutrition (TPN) for 10 days prior to surgery reduced postoperative complications in gastrointestinal cancer patients with severe undernutrition (defined as the serum albumin level  $< 30$  g/L or 15% weight loss during the past 6 months or BMI  $< 18$ ) [35]. Geisler et al. demonstrated that in 50% of the severe malnourished ovarian cancer patients showed nutritional improvement on TPN. This translated into less postoperative complications compared with those not responding to TPN [36].

Neoadjuvant chemotherapy offers an alternative approach for patients with nutritional compromise. After two to three cycles of neoadjuvant chemotherapy, the serum albumin level shows



improvement, patients start gaining weight, and their performance status improves [37]. This allows the surgeon to exercise maximum surgical efforts during delayed cytoreduction.

### **2.3. Tumor extent**

The relationship between tumor extent and tumor biology remains unclear. Eisenhauer et al. found that surgical resection counterweighed the presence of bulky upper abdominal disease and concluded that large tumor load did not indicate poor tumor biology [38]. Others, however, found that extensive disease cannot be “downgraded” by radical surgery and patients with high peritoneal cancer index will have poorer survival even if completely cytoreduced [39, 40]. Vergote et al. in their seminal EORTC55971 study found that patients with largest tumor diameter > 5 cm had better survival in the neoadjuvant chemotherapy arm [2]. It does not mean of course that maximum surgical effort should not be applied, as optimally cytoreduced patients consistently perform better than those with residual disease >1 cm [41]. In elderly or frail patients, however, even if it is technically resectable, four-quadrant disease distribution may render patients unsuitable for primary debulking surgery. Aletti et al. found in their study of patients with advanced ovarian cancer that those older than 75 years of age with high initial tumor load (or stage IV disease) plus poor performance or nutritional status were at significantly higher risk for postoperative complications with minimal survival benefit after undergoing complex radical surgery [42]. Delay in starting chemotherapy or dose delays occur more often in the elderly after primary debulking surgery, and this translates into poorer survival [43]. It is imperative, therefore, to find alternative treatment routes in elderly patients with large tumor volume and four-quadrant disease distribution. In such cases, neoadjuvant chemotherapy offers an effective and safe alternative.

### **2.4. Stage 4 disease**

Patients with stage 4 ovarian cancer represent a heterogeneous group with extraperitoneal metastases. According to recent FIGO staging, stage 4A includes patients with pleural effusion and positive peritoneal cytology. For note, the false-negative rate of pleural cytology is high; in a literature review on the use of video-assisted thoracoscopy in ovarian cancer patients with pleural effusion, 23% of the patients with negative pleural cytology had macroscopic disease found in the pleural cavity [44]. The presence of microscopic disease has not been assessed and can potentially be even more frequent. Patients with plural effusion represent a high-risk subgroup for postoperative complications with potential prolonged recovery and delayed administration of chemotherapy, and, therefore, application of neoadjuvant chemotherapy is a considerable strategy.

Stage 4B includes all other types of extraperitoneal metastases including splenic, hepatic, or lung parenchymal disease and lymph node metastases outside the abdominal cavity including the mediastinum, groin, axilla, and neck.

There seems to be an agreement that patients with stage 4 disease by virtue of solitary splenic parenchymal metastasis can easily be cytoreduced (dependent on the peritoneal disease of

course), so can be those with liver metastases in favorable anatomical positions. Controlling the peritoneal disease by complete cytoreduction in stage 4 disease appears to be associated with survival benefit [6]. This effect can only be observed in patients with complete macroscopic cytoreduction within the peritoneal cavity but not in those with any residual disease [45].

On the other hand, those with extensive mediastinal, axillary, or supraclavicular nodes or multiple, unresectable hepatic metastases represent a disease with different biological behaviors, and complete cytoreduction is not achievable; therefore, alternative treatment strategies must be considered [20, 21]. Furthermore, approximately 5% of the patients will progress through chemotherapy so patients with unresectable extraperitoneal disease should not be exposed to primary radical peritoneal resection [4, 17].

In these patients, neoadjuvant chemotherapy offers a safe and effective treatment alternative. Firstly, patients with platinum-refractory disease will not receive an unnecessary peritoneal surgical debulking with the associated morbidity. Furthermore, neoadjuvant chemotherapy effectively eliminates pleural effusion and ascites, improves performance status and serum albumin level, and, therefore, provides the surgeon with an opportunity to exercise maximum surgical effort with acceptable morbidity [37, 46].

The EORTC55971 trial confirmed that neoadjuvant chemotherapy results in superior survival compared with primary debulking surgery in the management of patients with stage 4 disease [2]. In such clinical scenario, the joint ASCO/SGO guideline also recommends the use of neoadjuvant chemotherapy [20, 21].

### 3. Conclusions

With no doubt, the presence of any residual disease after cytoreductive surgery remains the most important adverse prognostic factor that clinicians have to control over. Therefore, complete macroscopic clearance of the peritoneal cavity should always be the aim of surgery. Preoperatively, patients should undergo holistic assessment by gynecologic oncologist with regard of the disease distribution, extent, stage, and resectability; the patients' physical and emotional capacity to cope with the burden of surgery; and their nutritional status. All efforts should be focused on optimizing patients to tolerate the maximal surgical effort with acceptable morbidity and mortality. While primary debulking surgery remains the standard approach for patients with stage 3 ovarian cancer with optimal age, performance status, and nutritional status, there is growing evidence that neoadjuvant chemotherapy offers a safe and effective alternative for patients with less favorable characteristics.

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## References

- [1] Elattar A, Bryant A, Winter-Roach BA, Hatem M, Naik R. Optimal primary surgical treatment for advanced epithelial ovarian cancer. *Cochrane Database of Systematic Reviews*. 2011 Aug 10;8. DOI: CD007565
- [2] Vergote I, Tropé CG, Amant F, Kristensen GB, Ehlen T, Johnson N, Verheijen RH, van der Burg ME, Lacave AJ, Panici PB, Kenter GG, Casado A, Mendiola C, Coens C, Verleye L, Stuart GC, Pecorelli S, Reed NS; European Organization for Research and Treatment of Cancer-Gynaecological Cancer Group; NCIC Clinical Trials Group. Neoadjuvant chemotherapy or primary surgery in stage IIIc or IV ovarian cancer. *The New England Journal of Medicine* 2010 Sep 2;**363**(10):943-953
- [3] du Bois A, Reuss A, Pujade-Lauraine E, Harter P, Ray-Coquard I, Pfisterer J. 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 Mar 15;**115**(6):1234-1244
- [4] Kehoe S, Hook J, Nankivell M, Jayson GC, Kitchener H, Lopes T, Luesley D, Perren T, Bannoo S, Mascarenhas M, Dobbs S, Essapen S, Twigg J, Herod J, McCluggage G, Parmar M, Swart AM. Primary chemotherapy versus primary surgery for newly diagnosed advanced ovarian cancer (CHORUS): An open-label, randomised, controlled, non-inferiority trial. *Lancet*. 2015 Jul 18;**386**(9990):249-257
- [5] Winter WE 3rd, Maxwell GL, Tian C, Carlson JW, Ozols RF, Rose PG, Markman M, Armstrong DK, Muggia F, McGuire WP; Gynecologic Oncology Group Study. Prognostic factors for stage III epithelial ovarian cancer: A Gynecologic Oncology Group Study. *Journal of Clinical Oncology*. 2007;**25**:3621-3627
- [6] Winter WE 3rd, Maxwell GL, Tian C, Sundborg MJ, Rose GS, Rose PG, Rubin SC, Muggia F, WP MG, Gynecologic Oncology Group. Tumor residual after surgical cytoreduction in prediction of clinical outcome in stage IV epithelial ovarian cancer: A Gynecologic Oncology Group Study. *Journal of Clinical Oncology*. 2008;**26**:83-89
- [7] Chi DS, Eisenhauer EL, Zivanovic O, Sonoda Y, Abu-Rustum NR, Levine DA, Guile MW, Bristow RE, Aghajanian C, Barakat RR. Improved progression-free and overall survival in advanced ovarian cancer as a result of a change in surgical paradigm. *Gynecologic Oncology*. 2009 Jul;**114**(1):26-31
- [8] Rodriguez N, Miller A, Richard SD, Rungruang B, Hamilton CA, Bookman MA, Maxwell GL, Horowitz NS, Krivak TC. Upper abdominal procedures in advanced stage ovarian or primary peritoneal carcinoma patients with minimal or no gross residual disease: An analysis of Gynecologic Oncology Group (GOG) 182. *Gynecologic Oncology*. 2013 Sep;**130**(3):487-492
- [9] Vergote I, De Wever I, Tjalma W, Van Gramberen M, Decloedt J, van Dam P. Neoadjuvant chemotherapy or primary debulking surgery in advanced ovarian carcinoma: A retrospective analysis of 285 patients. *Gynecologic Oncology* 1998;**71**:431-436



- [10] Jacob JH, Gershenson DM, Morris M, Copeland LJ, Burke TW, Wharton JT. Neoadjuvant chemotherapy and interval debulking for advanced epithelial ovarian cancer. *Gynecologic Oncology*. 1991 Aug;**42**(2):146-150
- [11] Schwartz PE, Chambers JT, Makuch R. Neoadjuvant chemotherapy for advanced ovarian cancer. *Gynecologic Oncology*. 1994 Apr;**53**(1):33-37
- [12] Bristow RE, Chi DS. Platinum-based neoadjuvant chemotherapy and interval surgical cytoreduction for advanced ovarian cancer: A meta-analysis. *Gynecologic Oncology*. 2006 Dec;**103**(3):1070-1076
- [13] Querleu D, Planchamp F, Chiva L, Fotopoulou C, Barton D, Cibula D, Aletti G, Carinelli S, Creutzberg C, Davidson B, Harter P, Lundvall L, Marth C, Morice P, Rafii A, Ray-Coquard I, Rockall A, Sessa C, van der Zee A, Vergote I, du Bois A. European society of gynaecologic oncology quality indicators for advanced ovarian cancer surgery. *International Journal of Gynecological Cancer*. 2016 Sep;**26**(7):1354-1363
- [14] Fotopoulou C, Sehouli J, Aletti G, Harter P, Mahner S, Querleu D, Chiva L, Gabra H, Colombo N, du Bois A. Value of neoadjuvant chemotherapy for newly diagnosed advanced ovarian cancer: A European perspective. *Journal of Clinical Oncology* 2017 Feb 20;**35**(6):587-590
- [15] Dizon DS. Neoadjuvant chemotherapy for newly diagnosed ovarian cancer: It's all about selection. *Gynecologic Oncology*. 2017 Feb;**144**(2):241-242
- [16] Phillips A, Balega J, Nevin J, Singh K, Elattar A, Kehoe S, Sundar S. Reporting 'Denominator' data is essential for benchmarking and quality standards in ovarian cancer. *Gynecologic Oncology*. 2017 Apr 12 pii: S0090-8258(17)30786-2
- [17] Fagotti A, Ferrandina G, Vizzielli G, Fanfani F, Gallotta V, Chiantera V, Costantini B, Margariti PA, Gueli Alletti S, Cosentino F, Tortorella L, Scambia G. Phase III randomised clinical trial comparing primary surgery versus neoadjuvant chemotherapy in advanced epithelial ovarian cancer with high tumour load (SCORPION trial): Final analysis of peri-operative outcome. *European Journal of Cancer*. 2016 May;**59**:22-33
- [18] Onda T, Satoh T, Saito T, Kasamatsu T, Nakanishi T, Nakamura K, Wakabayashi M, Takehara K, Saito M, Ushijima K, Kobayashi H, Kawana K, Yokota H, Takano M, Takeshima N, Watanabe Y, Yaegashi N, Konishi I, Kamura T, Yoshikawa H. Japan Clinical Oncology Group. Comparison of treatment invasiveness between upfront debulking surgery versus interval debulking surgery following neoadjuvant chemotherapy for stage III/IV ovarian, tubal, and peritoneal cancers in a phase III randomised trial: Japan Clinical Oncology Group Study JCOG0602. *European Journal of Cancer*. 2016 Sep;**64**:22-31
- [19] Melamed A, Hinchcliff EM, Clemmer JT, Bregar AJ, Uppal S, Bostock I, Schorge JO, Del Carmen MG, Rauh-Hain JA. Trends in the use of neoadjuvant chemotherapy for advanced ovarian cancer in the United States. *Gynecologic Oncology*. 2016 Nov;**143**(2):236-240
- [20] Wright AA, Bohlke K, Armstrong DK, Bookman MA, Cliby WA, Coleman RL, Dizon DS, Kash JJ, Meyer LA, Moore KN, Olawaiye AB, Oldham J, Salani R, Sparacio D, Tew WP,

- Vergote I, Edelson MI. Neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer: Society of Gynecologic Oncology and American Society of Clinical Oncology Clinical Practice Guideline. *Gynecologic Oncology*. 2016 Oct;**143**(1):3-15
- [21] Wright AA, Bohlke K, Armstrong DK, Bookman MA, Cliby WA, Coleman RL, Dizon DS, Kash JJ, Meyer LA, Moore KN, Olawaiye AB, Oldham J, Salani R, Sparacio D, Tew WP, Vergote I, Edelson MI. Neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer: Society of Gynecologic Oncology and American Society of Clinical Oncology Clinical Practice Guideline. *Journal of Clinical Oncology*. 2016 Oct 1;**34**(28):3460-3473
- [22] Langstraat C, Aletti GD, Cliby WA. Morbidity, mortality and overall survival in elderly women undergoing primary surgical debulking for ovarian cancer: A delicate balance requiring individualization. *Gynecologic Oncology*. 2011 Nov;**123**(2):187-191
- [23] Mahdi H, Wiechert A, Lockhart D, Rose PG. Impact of age on 30-day mortality and morbidity in patients undergoing surgery for ovarian cancer. *International Journal of Gynecological Cancer*. 2015 Sep;**25**(7):1216-1223
- [24] Nisar PJ, Appau KA, Remzi FH, Kiran RP. Preoperative hypoalbuminemia is associated with adverse outcomes after ileoanal pouch surgery. *Inflammatory Bowel Diseases*. 2012;**18**:1034-1041
- [25] Hennessey DB, Burke JP, Ni-Dhonochu T, Shields C, Winter DC, Mealy K. Preoperative hypoalbuminemia is an independent risk factor for the development of surgical site infection following gastrointestinal surgery: A multi-institutional study. *Annals of Surgery*. 2010;**252**:325-329
- [26] Lohsiriwat V, Lohsiriwat D, Boonnuch W, Chinswangwatanakul V, Akaraviputh T, Lert-Akayamanee N. Pre-operative hypoalbuminemia is a major risk factor for postoperative complications following rectal cancer surgery. *World Journal of Gastroenterology*. 2008;**14**:1248-1251
- [27] Kudsk KA, Tolley EA, DeWitt RC, Janu PG, Blackwell AP, Yearly S, et al. Preoperative albumin and surgical site identify surgical risk for major postoperative complications. *Journal of Parenteral and Enteral Nutrition*. 2003;**27**:1-9
- [28] Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri SF. Preoperative serum albumin level as a predictor of operative mortality and morbidity—Results from the national VA surgical risk study. *Archives of Surgery*. 1999;**134**:36-42
- [29] Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P, DGEM (German Society for Nutritional Medicine), Jauch KW, Kemen M, Hiesmayr JM, Horbach T, Kuse ER, Vestweber KH, ESPEN (European Society for Parenteral and Enteral Nutrition). ESPEN Guidelines on Enteral Nutrition: Surgery including organ transplantation. *Clinical Nutrition*. 2006 Apr;**25**(2):224-244
- [30] Laky B, Janda M, Cleghorn G, Obermair A. Comparison of different nutritional assessments and body-composition measurements in detecting malnutrition among gynecologic cancer patients. *The American Journal of Clinical Nutrition*. 2008;**87**:1678-1685

- [31] Ataseven B, du Bois A, Reinthaller A, Traut A, Heitz F, Aust S, Prader S, Polterauer S, Harter P, Grimm C. Pre-operative serum albumin is associated with post-operative complication rate and overall survival in patients with epithelial ovarian cancer undergoing cytoreductive surgery. *Gynecologic Oncology* 2015 Sep; **138**(3):560-565
- [32] Uppal S, Al-Niaimi A, Rice LW, Rose SL, Kushner DM, Spencer RJ, Hartenbach E. Preoperative hypoalbuminemia is an independent predictor of poor perioperative outcomes in women undergoing open surgery for gynecologic malignancies. *Gynecologic Oncology*. 2013 Nov; **131**(2):416-422
- [33] Richardson DL, Mariani A, Cliby WA. Risk factors for anastomotic leak after rectosigmoid resection for ovarian cancer. *Gynecologic Oncology*. 2006 Nov; **103**(2):667-672
- [34] Obermair A, Hagenauer A, Tamandl D, Clayton RD, Nicklin JL, Perrin LC, Ward BG, Crandon AJ. Safety and efficacy of low anterior en bloc resection as part of cytoreductive surgery for patients with ovarian cancer. *Gynecologic Oncology*. 2001; **83**:115-120
- [35] Bozzetti F, Gavazzi C, Miceli R, Rossi N, Mariani L, Cozzaglio L, Bonfanti G, Piacenza S. Perioperative total parenteral nutrition in malnourished, gastrointestinal cancer patients: A randomized, clinical trial. *Journal of Parenteral and Enteral Nutrition*. 2000 Jan-Feb; **24**(1):7-14
- [36] Geisler JP, Linnemeier GC, Thomas AJ, Manahan KJ. Nutritional assessment using prealbumin as an objective criterion to determine whom should not undergo primary radical cytoreductive surgery for ovarian cancer. *Gynecologic Oncology*. 2007 Jul; **106**(1):128-131
- [37] Glaser G, Hartmann L, Cliby W, Torres M, Tabbaa Z, Kalli K, Weaver A, Jatoi A, Mariani A. Impact of neoadjuvant chemotherapy (NACT) on nutritional status and treatment-related morbidity in medically unfit women with advanced ovarian cancer (AOC). *Gynecologic Oncology*. March 2012; S101
- [38] Eisenhauer EL, Abu-Rustum NR, Sonoda Y, Levine DA, Poynor EA, Aghajanian C, Jarnagin WR, DeMatteo RP, D'Angelica MI, Barakat RR, Chi DS. The addition of extensive upper abdominal surgery to achieve optimal cytoreduction improves survival in patients with stages III-IV epithelial ovarian cancer. *Gynecologic Oncology*. 2006 Dec; **103**(3):1083-1090
- [39] Eisenkop SM, Spirtos NM. Procedures required to accomplish complete cytoreduction of ovarian cancer: Is there a correlation with "biological aggressiveness" and survival? *Gynecologic Oncology*. 2001 Sep; **82**(3):435-441
- [40] Martinez A, Ngo C, Leblanc E, Gouy S, Luyckx M, Darai E, Classe JM, Guyon F, Pomel C, Ferron G, Filleron T, Querleu D. Surgical complexity impact on survival after complete cytoreductive surgery for advanced ovarian cancer. *Annals of Surgical Oncology*. 2016 Aug; **23**(8):2515-2521
- [41] Eisenkop SM, Spirtos NM, Friedman RL, Lin WC, Pisani AL, Peticucci S. Relative influences of tumor volume before surgery and the cytoreductive outcome on survival

for patients with advanced ovarian cancer: A prospective study. *Gynecologic Oncology*. 2003 Aug;**90**(2):390-396

- [42] Aletti GD, Eisenhauer EL, Santillan A, Axtell A, Aletti G, Holschneider C, Chi DS, Bristow RE, Cliby WA. Identification of patient groups at highest risk from traditional approach to ovarian cancer treatment. *Gynecologic Oncology*. 2011 Jan;**120**(1):23-28
- [43] Joseph N, Clark RM, Dizon DS, Lee MS, Goodman A, Boruta D Jr, Schorge JO, Del Carmen MG, Growdon WB. Delay in chemotherapy administration impacts survival in elderly patients with epithelial ovarian cancer. *Gynecologic Oncology* 2015 Jun;**137**(3):401-405
- [44] Di Guilmi J, Salvo G, Mehran R, Sood AK, Coleman RL, KH L, Vaporciyan A, Ramirez PT. Role of video-assisted thoracoscopy in advanced ovarian cancer: A literature review. *International Journal of Gynecological Cancer*. 2016 May;**26**(4):801-806
- [45] Wimberger P, Wehling M, Lehmann N, Kimmig R, Schmalfeldt B, Burges A, Harter P, Pfisterer J, du Bois A. Influence of residual tumor on outcome in ovarian cancer patients with FIGO stage IV disease: An exploratory analysis of the AGO-OVAR (Arbeitsgemeinschaft Gynaekologische Onkologie Ovarian Cancer Study Group). *Annals of Surgical Oncology* 2010 Jun;**17**(6):1642-1648
- [46] Hou JY, Kelly MG, Yu H, McAlpine JN, Azodi M, Rutherford TJ, Schwartz PE. Neoadjuvant chemotherapy lessens surgical morbidity in advanced ovarian cancer and leads to improved survival in stage IV disease. *Gynecologic Oncology*. 2007 Apr;**105**(1):211-217

