Primary Surgical Treatment of Epithelial Ovarian Cancer

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Abstract

The main purpose of primary surgery for ovarian cancer is to eradicate the tumor completely because the postoperative residual tumor diameter is correlated with the prognosis. Surgery after neoadjuvant chemotherapy should be considered for patients with advanced cancer in whom complete tumor resection cannot be expected because of extensive peritoneal spread as well as patients whose general condition is poor. Recently it is also an acceptable alternative for women with potentially resectable disease who prefer the neoadjuvant approach because neoadjuvant chemotherapy plus subsequent surgery is not inferior to primary surgery in terms of progression-free survival or overall survival. Centralizing the primary care of advanced ovarian cancer to high-volume hospitals also increases the frequency of achieving complete cytoreduction with surgery and significantly improves survival. Although lymphadenectomy is essential for accurate staging of patients, there have been no reports showing therapeutic efficacy of lymphadenectomy. We are waiting for the results of Arbeitsgemeinschaft Gynäkologische Onkologie (AGO) clinical studies to decide the role of lymphadenectomy in advanced ovarian cancer.

Keywords

Primary debulking surgery (PDS) • Interval debulking surgery (IDS) • Neoadjuvant chemotherapy (NAC) • Centralized primary care • Lymphadenectomy • Fertility-preserving surgery

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11.1 Introduction

The aims of primary surgery for ovarian cancer are (1) to determine the tumor histology and the International Federation of Gynecology and Obstetrics (FIGO) stage, (2) to completely eradicate the tumor, and (3) to obtain information on prognostic factors.

The following surgical methods are employed to achieve these objectives:

1. Standard surgery: bilateral salpingo-oophorectomy + hysterectomy + omentectomy
2. Staging laparotomy: includes sufficient surgical procedures to determine the FIGO stage
3. Exploratory laparotomy: minimal surgery to determine the FIGO stage when it is impossible to remove the tumor completely
4. Debulking surgery: involves removing the tumor as completely as possible
   (a) Primary debulking surgery (PDS) is performed to remove the tumor as completely as possible before other treatment.
   (b) Interval debulking surgery (IDS) is performed to remove the tumor as completely as possible as a secondary procedure after chemotherapy.
   (c) Secondary debulking surgery (SDS) is performed to remove recurrent tumors as completely as possible (including surgery for residual tumors after completion of primary chemotherapy).

The concept of cytoreduction involves removing a malignant tumor as completely as possible, while debulking involves performance of surgical cytoreduction to enhance the effect of chemotherapy by making the tumor volume as small as possible. Thus, "debulking" surgery is similar to "cytoreductive" surgery and is classified into the following three types:

1. Complete surgery: no residual tumor detectable by macroscopic examination
2. Optimal surgery: maximum residual tumor diameter <1 cm
3. Suboptimal surgery: maximum residual tumor diameter ≥1 cm

The completeness of surgery is the most important prognostic factor for patients with ovarian cancer, and the postoperative residual tumor diameter is correlated with the prognosis, especially in patients with advanced cancer [1–4]. Therefore, surgical treatment of this disease should generally involve PDS aimed at complete removal of all lesions. However, performing IDS after several cycles of NAC should be considered for patients with advanced cancer in whom complete tumor resection cannot be expected because of extensive peritoneal dissemination and metastasis, as well as patients with massive ascites, patients whose general condition is poor, and patients with serious complications such as thrombosis. Several randomized trials have recently compared NAC + IDS with PDS to assess the usefulness of NAC for advanced cancer. It is also an acceptable alternative for women with potentially resectable disease who prefer the neoadjuvant approach, as new guidelines indicate that NAC + subsequent surgery is not inferior to surgery in terms of progression-free survival or overall survival [5].

Along with achieving complete tumor resection at primary surgery, it is well known that treatment at a high-volume hospital has a survival benefit for patients with advanced ovarian cancer [6, 7]. Centralizing the primary care of advanced ovarian cancer to high-volume hospitals increases the frequency of achieving complete cytoreduction with PDS, shortens the interval between PDS and initiation of chemotherapy, and significantly improves survival.

The Japan Society of Gynecologic Oncology (JSGO) recently revised its Ovarian Cancer Treatment Guidelines and released the 4th version in 2015 [8]. While the Guidelines state that lymphadenectomy is essential for accurate staging of patients with early ovarian cancer, there have been no reports of randomized controlled trials showing therapeutic efficacy of lymphadenectomy. In patients with advanced disease, lymphadenectomy should also be considered if optimal debulking has been performed, but there is again no evidence of its therapeutic efficacy. We are waiting for the results of AGO (Arbeitsgemeinschaft Gynäkologische Onkologie) clinical studies to decide the role of lymphadenectomy.

Whenever possible, fertility-preserving surgery must be performed without compromising complete tumor removal and staging, taking into consideration the patient's histopathological/clinical status. However, it is difficult to conduct clinical studies on this type of surgery, as we discuss later in this article.

11.2 Centralized Primary Care for Advanced Ovarian Cancer

Ovarian cancer is a complex and often advanced disease that requires multidisciplinary expert surgical and medical management to provide state-of-the-art care, along with counseling, access to clinical trials, and a wealth of experience. Optimum management requires "the skillful and appropriate integration of cancer surgery and chemotherapy and is best carried out in centers in which an experienced and coordinated multidisciplinary team is available". Many studies have shown that outcomes are improved when ovarian cancer is treated in high-volume and/or specialist centers [9–12]. The Swedish study [6] assessed the effects of sweeping, regional, population-based changes to ovarian cancer management in western Sweden by comparison of outcomes between two different periods, which were 2008–2010 (prior to centralization of care for ovarian cancer) versus 2011–2013 (after centralization). This study revealed several important improvements of outcomes, e.g., there was a higher complete cytoreduction rate at primary surgery (37% versus 49%; $p = 0.03$) and a decrease of the interval from surgery to chemotherapy (36 versus 24 days; $p = 0.01$). Despite the two cohorts receiving similar chemotherapy regimens, there was also a slightly higher completion rate of planned chemotherapy with centralized care (88% versus 92%; p: 0.18). The most impressive finding was the increase of the 3-year survival rate in patients with advanced disease undergoing PDS, which rose from 44% to 65% after centralization, along with an estimated 42% decrease of the excess mortality rate ratio (EMRR) (RR: 0.58; 95% CI: 0.42–0.79). Even though use of NAC increased in the second period, when the entire cohort was compared irrespective of primary treatment, the 3-year survival rate still increased from 40% to 61% and EMRR declined (RR: 0.59; 95% CI: 0.45–0.76).

These improvements are consistent with the findings obtained by retrospective studies on the quality of care and outcomes using public databases [9–12]. Thus, management at expert centers improves outcomes, but centralization of care is a long and difficult process which must include professional societies, politicians, clinicians, epidemiologists, payers, and advocates.

11.3 Optimal Surgical Management of Ovarian Cancer Clinically Confined to the Ovary

Even when a lesion is expected to be confined to the ovary, peritoneal dissemination and retroperitoneal lymph node metastasis may be detected by staging laparotomy, resulting in a diagnosis of Stage II-III cancer. Accordingly, even in patients with early ovarian cancer whose disease is expected to be confined to the ovary, it is recommended that not only ipsilateral salpingo-oophorectomy but also contralateral salpingo-oophorectomy and total hysterectomy be performed to confirm the presence or absence of tumor metastasis and infiltration. In addition, intraperitoneal cytologic examination (sampling of ascites or lavage ascites) should also be performed together with omentectomy and peritoneal biopsy at various sites to confirm the presence or absence of intraperitoneal dissemination. Furthermore, taking the possibility of retroperitoneal lymph node metastasis into consideration, dissection or biopsy of the pelvic to para-aortic lymph nodes should be carried out. While this type of staging laparotomy is recommended for histopathological staging and identification of patients who do not require postoperative treatment, there is currently no evidence to indicate whether staging laparotomy itself directly improves the prognosis or not.

Because omental metastases are noted during surgery in 2–7% of patients with a clinical diagnosis of early ovarian cancer, partial omentectomy is also an essential part of management, even in patients with early disease [13].

For accurate staging, it is important to examine various intraperitoneal sites by biopsy. If tumor dissemination is suspected from the results of careful observation during laparotomy, it is recommended that peritoneal biopsy be performed at the pouch of Douglas, vesical peritoneum, right and left lateral pelvic walls, right and left paracolic sulci, and right diaphragm (although biopsy of the diaphragm may be replaced by scraping cytology). If mucinous carcinoma is suspected, appendectomy should be considered for differentiation from primary cancer of the appendix. While the significance of performing appendectomy in ovarian cancer patients has not been established, it has been reported that the incidence of metastasis to a macroscopically normal appendix is 2.8% [14].

11.4 Optimal Surgical Management of Clinical Stage II or More Advanced Ovarian Cancer

The fundamental surgical technique for advanced cancer is primary debulking surgery (PDS), which involves removal of intraperitoneal dissemination and metastases as completely as possible. It has been reported that the diameter of the residual

tumor is correlated with the prognosis, and it was recently shown that the prognosis is significantly better after complete surgery than optimal surgery [1–4]. However, it is rare for advanced cancer to be controlled by standard surgical management (bilateral salpingo-oophorectomy + total hysterectomy + omentectomy) alone. There is no standard PDS method for advanced cancer. Tumors are resected as completely as possible for debulking irrespective of the organ affected by dissemination/metastasis. Resection of peritoneal lesions at various sites (including the vesicouterine pouch, the pouch of Douglas, and the paracolic sulci) together with the surrounding peritoneum should be considered for control of dissemination and metastasis. If there is infiltration into the rectum at the pouch of Douglas, infiltration into the sigmoid colon, infiltration/extension of omental lesions into the transverse colon, or infiltration/metastasis affecting the small intestine, partial intestinal resection/reconstruction should be actively considered. If this is done, construction of colostomy may be required, depending on the site of bowel resection. In patients with mucinous carcinoma, appendectomy should be considered in order to detect primary cancer of the appendix [14]. If involvement of the diaphragm is noted, stripping or full-thickness resection should be considered, since the frequency of achieving complete surgery can be increased by resecting diaphragmatic lesions. If infiltration into the spleen is noted, splenectomy should also be considered .The diagnostic significance of retroperitoneal lymph node dissection and biopsy for accurate staging has been established, but the therapeutic significance is not necessarily clear.

Of course, the ability to remove tumors in patients with advanced ovarian cancer irrespective of the organs affected will depend on the skill of the surgeons and the facilities of the treating hospital (Sect. 11.3).

11.5 Neoadjuvant Chemotherapy (NAC) and Interval Debulking Surgery (IDS)

The standard treatment of stage IIIC or IV invasive epithelial ovarian cancer has generally been primary debulking surgery (PDS), followed by chemotherapy, and PDS is still preferred over NAC if there is a high likelihood of achieving residual disease <1 cm in diameter (ideally, no macroscopic disease).

On the other hand, NAC is the preferred treatment option for women with advanced ovarian cancer or related cancers if it is unlikely that PDS can reduce the residual disease to <1 cm in diameter. It is also an alternative approach to the management of potentially resectable disease, since it has been reported that NAC + subsequent surgery is not inferior to surgery with regard to either progression-free survival or overall survival [5]. Thus, women with potentially resectable disease may be offered either NAC or PDS, even if they are fit enough to undergo surgery, as their survival outcomes will be comparable. However, NAC should be the preferred option for women with high surgical risk or those in whom there is little likelihood of achieving residual disease <1 cm in diameter (or no macroscopic disease). The main advantage of NAC + IDS is less perioperative/postoperative morbidity or mortality than PDS, although PDS may achieve superior overall survival

in selected patients. Before NAC is commenced, all patients should have histologic confirmation (core biopsy is preferred) of the diagnosis of invasive ovarian cancer. If biopsy cannot be performed, the oncologist should carry out cytologic evaluation. Together with a serum CA-125/carcinoembryonic antigen ratio >25 [5], cytologic evaluation should confirm the primary diagnosis and exclude non-gynecologic cancer. IDS should be performed after a maximum of four NAC cycles in women who respond to treatment or achieve stable disease. In contrast, "patients with progressive disease on NAC have a poor prognosis". For these women, options include switching to an alternative chemotherapy regimen, referral to an appropriate clinical trial, or initiation of best supportive care. Surgery is not advised for these women unless it is required for palliative purposes. Laparoscopy or imaging studies may be performed for more detailed assessment, and whether a patient is eligible for medical or surgical treatment should only be decided in consultation with a gynecologic oncologist.

11.6 Lymph Node Metastasis in the New FIGO Ovarian Cancer Staging System (2014) [15]

Lymph node metastases are found in the majority of patients who undergo lymph node sampling or dissection and in up to 78% of patients with advanced disease. Approximately 9% of patients with tumors that appear to be stage I actually have lymph node metastases, while the corresponding figures for stages II, III, and IV are 36%, 55%, and 88%, respectively. Occasionally, inguinal or supraclavicular (stage IV) lymph node metastasis is the presenting manifestation of ovarian carcinoma. However, less than 10% of ovarian cancers extend beyond the pelvis with exclusively retroperitoneal lymph node involvement. Published evidence indicates that these patients just with lymph node metastasis have a better prognosis than that of patients with involvement of the abdominal peritoneum. The new staging system includes a revision of stage III and assigns patients to stage IIIA1 based on involvement of the retroperitoneal lymph nodes without intraperitoneal dissemination. Stage IIIA1 is further divided into IIIA1 (1) (metastasis ≤10 mm in greatest dimension) and IIIA1 (2) (metastasis >10 mm in greatest dimension), although there are no retrospective data supporting quantification of the size of metastasis. Involvement of retroperitoneal lymph nodes must be proven cytologically or histologically. In the future, we will need to compare outcomes between stage IIIA1 (1) and IIIA1 (2) patients as well as between stage IIIA1 and IIIA2 patients.

11.7 Lymphadenectomy for Early Ovarian Cancer

In 1988, the International Federation of Gynecology and Obstetrics published a surgical staging scheme for ovarian cancer that included pelvic and para-aortic lymph node sampling or lymphadenectomy. However, few studies have shown any benefit of lymphadenectomy in patients with early disease. Although systematic

Table 11.1 Frequency of lymph node metastasis in pT1 disease

Author	Year	Number of patients	Positive rate(%)	Stage (%)			Positive rate(%)	
				Ia	Ib	Ic	PEN	PAN
Sakuragi, et al	2000	78	5.1	3.2	–	6.4	0	5.1
Suzuki, et al	2000	47	10.6	5.6	–	13.8	8.5	4.3
Cass, et al	2001	96	14.5	–	–	–	9.4	7.3
Takeshima, et al	2001	156	12.8	9.3	33.3	15.4	7.1	9.6
Harter, et al	2007	48	6.2	0	25.0	8.0	–	–
Fournier, et al	2009	54	9.3	3.8	0	17.4	–	–
Nomura, et al	2010	60	13.3	28.6	0	9.1	8.3	11.7
Mikami, et al	2014	89	12.3	4	50	17.6	10.1	6.7

PEN pelvic lymphnode, *PAN* paraaortic lymphnodes

lymphadenectomy is necessary for accurate staging and has diagnostic value, it may increase surgical morbidity. Recently, Chan et al. [16] conducted a large-scale, retrospective study that assessed the impact of lymphadenectomy on survival in patients with clinical stage I ovarian cancer, and their findings suggested that lymphadenectomy significantly improved survival. In contrast, a randomized study of systematic lymphadenectomy in patients with pT1 and pT2 ovarian cancer [17] showed that lymphadenectomy had no influence on either progression-free survival or overall survival. Involvement of pelvic nodes has been reported in 5–14% of patients with pT1 disease, and the para-aortic nodes are involved in 4–12% of these patients (Table 11.1.). The chief value of systematic retroperitoneal node dissection may be the upstaging of some patients with clinical stage I cancer, which leads them to receive postoperative chemotherapy. Also, when the initial staging is confirmed to be correct, patients with low-risk disease can avoid undergoing cytotoxic chemotherapy. Therefore, it can be argued that lymphadenectomy is essential to allow accurate staging of the tumor in patients with early ovarian cancer, although there is no supporting evidence from randomized trials.

Accordingly, surgical treatment of ovarian cancer, including systematic lymphadenectomy, should only be performed at institutions that specialize in gynecologic oncology, in order to ensure accurate staging of the tumor.

11.8 Lymphadenectomy for Advanced Ovarian Cancer: Complete Dissection Versus Resection of Bulky Nodes

Primary debulking surgery has been an integral part of treating advanced ovarian cancer. However, it is still unclear whether systematic resection of the retroperitoneal lymph nodes should be part of maximal debulking surgery, and the therapeutic value of systematic lymphadenectomy for women with advanced ovarian cancer remains controversial. Retrospective studies [18] have suggested that systematic lymphadenectomy significantly improves survival in patients undergoing debulking surgery for advanced disease, but no prospective studies have been reported. Panici

et al. [19] performed a multicenter randomized clinical trial that revealed significant improvement of progression-free survival by systematic lymphadenectomy, although overall survival was similar between patients receiving systematic lymphadenectomy and those undergoing resection of bulky nodes. They also reported a higher rate of lymph node metastasis in the patients receiving systematic lymphadenectomy than in those having resection of bulky nodes and confirmed that lymph node metastasis is a significant prognostic factor for survival. Furthermore, du Bois [20] reviewed three prospective randomized trials of platinum/taxane-based chemotherapy for advanced ovarian cancer and concluded that lymphadenectomy might mainly benefit patients with advanced disease who underwent complete intraperitoneal debulking. However, this conclusion needs to be confirmed by performing a further prospective randomized trial. In these three trials, 24.8% of patients who underwent pelvic and para-aortic lymphadenectomy without suspected intraoperative lymph node involvement had histologically positive nodes, whereas the rate was 17.1% in patients who underwent partial retroperitoneal lymphadenectomy. This suggests that almost one third of positive nodes are not detectable clinically and may also be missed by partial lymphadenectomy. A prospective randomized trial comparing complete intraperitoneal tumor resection with or without sampling of suspicious lymph nodes in patients with advanced ovarian cancer (Lymphadenectomy In Ovarian Neoplasms [Lion] trial) is underway, and the results will hopefully shed new light on this important issue. Accordingly, systemic pelvic and para-aortic lymphadenectomy should be considered in patients who are fit to receive optimal debulking surgery.

11.9 Can Interval Debulking Surgery (IDS) Be Recommended After Primary Debulking Surgery (PDS) with a Suboptimal Outcome?

The usefulness of interval debulking surgery (IDS) during chemotherapy has been investigated for patients in whom the maximum residual tumor diameter could not be decreased to ≤1 cm by suboptimal primary surgery. Conflicting results have been obtained, with improvement of the prognosis in one study [21] and no benefit in another study [22], so there is no consensus as to whether IDS is useful for improving the prognosis of these patients. Study European Organization for Research and Treatment of Cancer-Gyne Cancer Group (EORTC-GCG) [21] enrolled 425 patients with Stage IIb-IV advanced ovarian cancer in whom the maximum tumor diameter was ≥1 cm at primary surgery, and tumor reduction (complete or partial response) was achieved in 319 patients by 3 cycles of combination chemotherapy with cyclophosphamide + cisplatin. These 319 patients were subjected to randomized comparison of the influence of IDS on the prognosis, revealing that overall survival was 33% higher in the IDS group compared with the non-IDS group. In Study GOG152 [22], the usefulness of IDS was assessed in 550 Stage III-IV ovarian cancer patients with suboptimal primary debulking surgery. A total of 448 patients received 3 cycles of post-PDS chemotherapy with paclitaxel + cisplatin and were randomized to two

groups that were treated by chemotherapy alone or IDS followed by chemotherapy. As a result, both progression-free survival and overall survival showed no significant difference between the two groups. These two randomized comparative trials yielded different results, presumably because there was a higher percentage of Stage IV patients and the residual tumor diameter was larger after primary surgery in Study EORTC-GCG, while a higher percentage of patients received PDS from gynecologic oncologists, and the residual tumor diameter was smaller in the Gynecologic Oncology Group (GOG) study. In other words, it seems likely that IDS is more closely related to improvement of the prognosis in patients with a larger residual tumor diameter after primary surgery.

11.10 Optimal Management for Preservation of Fertility

There are histopathological and clinical requirements to consider with regard to preserving fertility in patients with ovarian cancer. Histopathologically, preserving fertility is indicated for patients with Stage Ia Grade 1 or 2 serous carcinoma, mucinous carcinoma, or endometrioid carcinoma (non-clear), while it can be considered for non-clear Stage Ic (localized to one ovary with negative in ascites cytology) Grade 1 or 2 or Stage Ia clear cell carcinoma.

After fertility-preserving surgery, the recurrence rate of ovarian cancer was 5.2%, 20%, and ≥50% for Stage Ia patients with Grade 1, 2, and 3 disease, respectively, while it was 8%, 21%, and 33% for Stage Ic patients with the respective grades. These results are considered to confirm the above histopathological conditions for preserving fertility [23, 24]. However, fertility preservation should be selected with great care, because investigation of 29 Stage Ic patients revealed that the recurrence rate was higher in patients with positive ascites cytology or patients with infiltration into the capsule [25]. Because it is impossible for rapid intraoperative histopathological examination to evaluate all of the necessary factors, including the histologic type and differentiation, it is necessary to await the results of accurate postoperative histopathological diagnosis.

Importance must also be attached to the following clinical factors. (1) The patient has a strong desire for pregnancy and is of childbearing age. (2) The patient and her family fully understand the nature of ovarian cancer and fertility-preserving surgery, as well as the risk of recurrence. (3) The patient agrees to receive strict long-term follow-up after surgery. (4) The patient can undergo careful intraperitoneal exploration by a skillful gynecologic oncologist. Prior to surgery, it must also be explained fully that preservation of fertility might be impossible and reoperation (2-stage surgery) might be needed, depending on the results of postoperative histopathological examination. Because recurrence even 10 years postoperatively has been reported, it is also necessary to discuss possible completion of surgery after delivery [26].

For fertility-preserving surgery, the basic procedure includes ipsilateral salpingo-oophorectomy and omentectomy. Endometrial curettage must also be considered to exclude concurrent endometrial cancer [27, 28]. Accurate staging is required when selecting patients who can be considered for fertility-preserving surgery. Omission

of any of the procedures in staging laparotomy can only be considered when very careful macroscopic observation and palpation reveal nothing abnormal. Microscopic metastasis to the contralateral ovary has been reported to be rare in patients with Grade 1 ovarian cancer in whom macroscopic observation reveals no infiltration of the capsule surface, capsule disruption, or peritoneal dissemination. To avoid infertility due to decreased ovarian reserve and postoperative adhesions, it is permissible to omit biopsy of a macroscopically normal contralateral ovary. Concerning retroperitoneal lymph node dissection, it has been reported that the frequency of metastasis is low if the patient has mucinous carcinoma or endometrioid carcinoma and if there is no intrapelvic invasion or peritoneal dissemination [27]. Because fertility may be disturbed by postoperative adhesions due to lymph node dissection, it is permissible to limit examination to biopsy or lower levels if the clinical probability of metastasis is low.

Since the prognosis of the disease after recurrence is generally poor [29], very careful attention to management and providing adequate information for patients are essential.

11.11 Surgery for Elderly Patients

It is thought that maximal debulking surgery should also be performed in elderly patients with the aim of achieving complete resection, although the age range corresponding to "elderly" is not well defined. It is important to plan surgery by taking the patient's general condition, nutritional status, and complications into consideration. Caution must be exercised when performing surgical treatment on elderly patients because the incidence of intraoperative complications is higher and perioperative complications are also more frequent due to cardiac dysfunction [30]. The 30-day mortality rate after ovarian cancer surgery gradually increases with age from <70 years old to 70–79 years and then >80 years, with the causes of death including postoperative infection, hemorrhage, respiratory failure, heart failure, and thromboembolism. The incidence of perioperative complications increases as surgery becomes more complex due to addition of partial bowel resection, diaphragmatic resection, and/or splenectomy to the standard procedure of bilateral salpingo-oophorectomy + total hysterectomy + omentectomy. The best surgical procedure should be selected by considering the patient's age, general condition, nutritional status, and tumor stage at the time of diagnosis. The general condition is evaluated by determining the performance status (PS) (Table 11.2) and by using the American Society of Anesthesiologists (ASA) physical status classification (Table 11.3). Special care must be taken when the general condition corresponds to ASA Class 3 or higher (equivalent to a PS of 3 or higher) and the nutritional status is poor (serum albumin <3.0 g/dL), as well as when surgery is performed for Stage III or IV cancer [30]. In these patients, NAC should be performed before surgery is considered. After improvement of the general condition and the nutritional status, complete surgery can be performed as IDS [31]. However, performing NAC also requires care in the elderly because of the risk of complications such as thrombosis.

Table 11.2 ECOG performance status. Reuse from http://ecog-acrin.org/resources/ecog-performance-status, with permission

Developed by the Eastern Cooperative Oncology Group, Robert L. Comis, MD, Group Chair.[a]	
Grade	ECOG performance status
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities, up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled, cannot carry on any selfcare; totally confined to bed or chair
5	Dead

[a]Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*. 1982;5:649–655

Table 11.3 ASA physical status classification system. Reuse from https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system with permission

Last approved by the ASA House of Delegates on October 15, 2014		
Current definitions (NO CHANGE) and Examples (NEW)		
ASA PS Classification	Definition	Examples, including, but not limited to:
ASA I	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30 < BMI < 40), well-controlled DM/HTN, mild lung disease
ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA < 60 weeks, history (>3 months) of MI, CVA, TIA, or CAD/stents.
ASA IV	A patient with severe systemic disease that is a constant threat to life	Examples include (but not limited to): recent (<3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis
ASA V	A moribund patient who is not expected to survive without the operation	Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction
ASA VI	A declared brain-dead patient ASA VI whose organs are being removed for donor purposes	

11.12 Is Laparoscope-Assisted Surgery Possible?

The survival rate of patients with early ovarian cancer may be similar between after laparoscope-assisted staging surgery and laparotomy if these procedures are performed by skillful gynecologic oncologists [32, 33]. Laparoscopy is useful for observing intraperitoneal lesions and for staging in patients with advanced ovarian cancer or patients with incomplete primary surgery [33, 34]. Many studies have demonstrated that the upstaging rate is similar with these two procedures, and carbon dioxide pneumoperitoneum is considered to have no adverse influence on the survival of patients with advanced ovarian cancer and intraperitoneal metastases. However, it was reported that the incidence of tumor capsule rupture is higher with laparoscopy than laparotomy [35] and metastasis has occurred at the site of trocar insertion, so it cannot be concluded that laparoscope-assisted surgery is superior to laparotomy. Furthermore, although laparoscope-assisted surgery is considered to be a useful alternative to laparotomy for performing intraperitoneal observation/tissue sampling in patients with advanced ovarian cancer, it is not currently recommended for tumor debulking surgery. Only a few randomized trials of laparoscope-assisted surgery for ovarian cancer have been conducted, so there is little scientific evidence regarding its usefulness, and the indications for this technique are very limited.

Characteristically, rapid histopathological diagnosis is required during ovarian cancer surgery to determine whether the operative field should be extended or not. Because tumor capsule disruption may occur (possible iatrogenic upstaging) during surgery and because exploratory laparotomy with or without combined resection may be required for advanced cancer patients, it is relatively difficult to employ laparoscope-assisted surgery as an alternative to standard laparotomy. These factors also make it difficult to perform large-scale clinical studies for comparison of laparoscopy with laparotomy, and there have been no randomized comparison trials evaluating laparoscopic surgery for ovarian cancer. While the safety and efficacy of laparoscopic procedures have been reported in selected patients, there are still many problems to be solved such as lack of sufficient data to demonstrate a comparable survival rate. Therefore, it is still unclear whether laparoscope-assisted procedures can be introduced as primary standard surgery for ovarian cancer.

Conclusion

The completeness of surgery is the most important prognostic factor for patients with ovarian cancer, and the postoperative residual tumor diameter is correlated with the prognosis, especially in patients with advanced cancer. Increased use of NAC in women with advanced stage ovarian cancer has contributed to improved quality of life and reduced perioperative morbidity. However, questions remain about how to identify which patients are most likely to benefit from NAC. The creative strategies should be needed to triage patients between PDS and NAC. To shed light on these points, researchers should be exploring tumor markers and molecular pathways associated with invasive metastatic behavior.

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