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Review

Ovarian cancer: Is an expert surgical oncologist mandatory?

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Abstract

Ovarian cancer has the worst prognosis of all gynecologic malignancies. The standard treatment of patients with ovarian cancer is a multidisciplinary assignment involving aggressive surgery with or without chemotherapy.

Among the prognostic factors, the residual disease is of capital importance. Surgical outcomes, including the amount of residual disease, would be better if the surgical oncologist performed it. This optimal surgical treatment according to guidelines may provide the most important benefit in survival.

This current review aims at highlighting the positive relationship between complete cytoreductive surgery and survival.

Patients with OC should be referred to surgical oncologists providing high-quality comprehensive care.

Keywords : ovarian cancer, surgical oncologists, surgical outcomes, staging, cytoreduction, survival

Highlights

- ✓ Current literature data show that the specializations of the gynecologist and hospital are correlated with appropriately staged and optimally cytoreductive surgery in ovarian cancer.
- ✓ We suggest that patients with an early and advanced stage should be referred to specialized centers to ensure high-quality comprehensive care, including surgery and chemotherapy.

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Introduction

Ovarian cancer (OC) has the worst prognosis of all gynecologic malignancies (1). The standard care consists of aggressive surgery and chemotherapy. Surgery is essential in determining the correct stage of the disease and in achieving an optimal cytoreduction (2). In all the stages of the disease, patients treated by surgical oncologists (SOs) more often received adequate surgical care according to guidelines (1). The SO is a surgeon who has received special training in the management of OC including upper abdominal surgery. The residual disease is one of the most important prognostic factors (3). The literature data suggest a positive correlation between total cytoreductive surgery and survival (4, 5). The aim of the current literature is to answer the question: Is a specialist mandatory while dealing with OC?

Materials and Methods

Our literature search was conducted using PubMed, ScienceDirect and Google Scholar. We selected 48 articles in English and French from 1975 to 2018. The inclusion criteria were the presence of enough data allowing us to compare disease staging and/or cytoreductive surgery and/or mean survival and/or recurrence-free survival. We reviewed the published articles by using the following keywords: ovarian cancer, surgical oncologists, surgical outcomes, staging, cytoreduction, survival.

Results

1. The staging of the disease:

Lymph node involvement in an early stage of OC ranges from 4 to 25% (6, 7), showing the importance of lymph node assessment in the staging procedure.

Engelen et al. (1) demonstrated that patients with stage I-II disease seen by SOs more likely underwent omentectomy and lymphadenectomy compared to those treated by general gynecologists. In the same light, Marth et al. (3) found that the number of lymph nodes removed was more significant in large departments.

Therefore, SOs carry out a comprehensive staging more often than other surgeons (8–10).

Previous studies have reported that adequate staging involving extensive surgical procedure leads to stage migration to a more advanced stage of OC (11, 12).

Kumpulainen et al. estimated that women seen by other surgeons had a fourfold higher risk of having under staged disease (13). Similarly, in a study conducted by Carney et al. (14), the local-stage disease was diagnosed in 25.8% of the patients seen by SOs, and 30.7% in patients seen by non-SOs, thus representing the risk of under staging by non-SOs.

Furthermore, Carney et al. (14) found that 0.9% of the cases seen by a SO were classified with unknown stage disease. In contrast, 5.6% of the cases were classified with unknown stage disease if not treated by a SO.

Consequently, this may lead to under-treatment. Engelen et al. (1) reported that 85% of the patients treated by SOs received adjuvant chemotherapy when indicated, compared to 75% when seen by general gynecologists.

2. Cytoreductive surgery:

The primary goal of OC surgery should be the complete resection of all macroscopic disease or, if this is not possible, the smallest resection of the residual disease (15).

Moreover, in a retrospective multicenter cohort study including 1,290 patients, Glehen et al. considered the completeness of cytoreduction as an independent prognostic indicator (16–18).

Several studies advocated that women diagnosed with advanced OC benefit the most from oncologic units where maximal cytoreduction is achieved (18–25).

Besides, Engelen et al. found that 62% of the patients with FIGO stage III underwent complete debulking by SOs, compared to 45% of the patients who underwent surgery by general gynecologists (1). Similarly, Aletti et al. demonstrated that women treated by SOs were more likely to obtain complete debulking to less than 1cm of the residual disease (26).

Eisenkop et al. (20) found that the rate of maximal cytoreduction for SOs was 81.7% compared to 37.8% of those treated by general gynecologists. Olaitan et al. demonstrated that SOs were 2.06 times more likely to achieve optimal cytoreduction (27). Bailey et al. (28) and Junor et al. (19) had also reached the same conclusions.

In a retrospective cohort study conducted by Vernooij (29), 37% of the patients with stage III OC were debulked entirely in non-specialized hospitals, compared to 48% of the patients in specialized ones. Besides, low-volume gynecologists optimally debulked 37% of the patients with stage III disease, compared to 57% of those operated on by high-volume gynecologists. This study concluded to a positive correlation between the specialization of the hospital, the operative volume of the gynecologists and the percentage of optimally debulked patients.

Similarly, Marth et al (3) noticed that the complete debulking with no macroscopic residual disease was performed most frequently in large departments. A macroscopic residual disease of up to 1 cm was registered in 11% and 27% of the cases in large and small departments, respectively. Correspondingly, Marx et al.

(30) and Kumpulainen et al. (31) demonstrated that SOs and significant hospitals achieved better rates of complete or maximal cytoreduction compared to general gynecologists or non-specialized settings.

Moreover, Olsen et al. (2) have shown that surgeons in specialized hospitals were more experienced in the selection of women for surgery or neoadjuvant chemotherapy, which could support the better rate of complete cytoreductive surgery in specialized hospitals.

3. Survival

OC has a poor prognosis, being the most common cause of death due to gynecologic malignancies (15).

Nonetheless, adequate surgical staging, optimal tumor cytoreduction, and the selection of patients for chemotherapy have been shown to improve the overall survival rate of this disease (14).

Moreover, other authors stated that the care provided by SOs is the most predictive factor in the improvement of survival (23, 32).

Furthermore, increased risks of disease recurrence and mortality were associated with the treatment provided by inexperienced surgeons (33).

In fact, in a case-control study by Tingulstad et al., the median survival rate was 21 months for SO patients versus 12 months for those operated on by gynecologists (18). Junor et al. (19) have demonstrated a 6- to 9-month median survival advantage for patients operated on by SOs (P values 0.009 to 0.01). Moreover, some studies concluded that this improved survival rate was independent from chemotherapy (18, 34).

Besides, a positive relationship between the experience of the surgeon, the high-volume hospitals and the survival of patients with OC has been suggested (4, 5, 35, 36). Paulsen et al. have also mentioned that from the overall number of women with OC (198), those operated on by SOs had a 20% increased short-term survival rate (37).

In the ACTION trial (38), patients with the optimal staging presented an overall survival similar to patients with sub-optimal staging who received adjuvant chemotherapy. There was no additional survival benefit noticed when patients with optimal staging received adjuvant chemotherapy.

Furthermore, a statistically significant survival advantage was seen in 39.3% of the patients operated on by SOs in a study conducted by Carney et al. (14). They demonstrated an improvement in the median survival from 17 to 39 months when an optimal debulking was achieved (14). Engelen et al. had also noticed that the five-year survival rate of patients with stage III was 54% for those with no residual disease, 15% when residual disease masses measuring ≤ 2 cm, and 6% in case of higher masses of residual disease (1).

Consequently, the observed survival advantage may result from more aggressive surgeries done by SOs, allowing maximal cytoreductions (15, 18).

Similarly, Marth et al. demonstrated that each 10% increase in the maximal percentage cytoreductive surgery was associated with a 5.5% increase in the median survival time (3).

Furthermore, a prospective study by Eisenkop et al. (20) showed that the cytoreduction to macroscopically disease-free status has a more significant impact on survival than the extent of metastatic disease before surgery. On the other hand, Bristow et al. expected that the surgical expertise could partially overcome tumor grading and histological subtypes (39).

In a prospective quality assurance program conducted by Marth et al., survival was significantly longer in large departments than in small ones, with a 5-year survival rate of 69% and 61%, respectively for all the stages (3).

Correspondingly, Kumpulainen et al. (13) have shown that the five-year survival was better in university hospitals and hospitals with a more significant operative volume than in the rest of the hospitals. Birkmeyer et al. have also concluded that high-volume hospitals have better late survival rates than low-volume ones (40). Paulsen et al. (37) demonstrated similar results related to the optimal debulking of the tumor which was achieved in 30% of the patients operated on in teaching hospitals compared to 17% in non-teaching hospitals.

However, there is a controversy concerning this survival benefit in early-stage diseases. Engelen et al. found that the 5-year survival rate for patients with FIGO stage I–II OC was 86% when a SO performed surgery, whereas it was 70% when a general gynecologist performed it (1).

According to Marth et al., the overall survival was similar whether treated in large or small departments at FIGO stage I, whereas at FIGO stage II, the difference in survival did not have any statistical significance (3).

Previous studies have also found a non-statistically significant survival benefit for patients with early-stage disease operated on by SOs (14, 18).

Correspondingly, Craney et al. did not observe any statistically significant difference in survival between those seen or not by a SO for patients diagnosed with local and regional disease compared to those with distant disease (14). Chan et al. (36) have also observed that this survival advantage of patients operated on by SOs was more notable in those with stage III-IV disease (31.0% versus 22.5%;

P.001) with a non-significant survival improvement in early-stage disease (66.3% versus 61.1%; P.157).

Several studies have supported a decreased recurrence rate in patients with early-stage disease, receiving comprehensive staging (8, 10, 25).

Furthermore, Munstedt et al. (24) have stated that the treatment carried out by the general gynecologist was associated with increased risks of disease recurrence and mortality.

Moreover, Elit et al. noticed a decreased relative risk of re-operation in patients treated by SOs; the RR of re-operation was 0.04 (0.01–0.12) for SOs, in contrast with 0.37 (0.21–0.66) for gynecologists (35).

In a multivariable analysis by Vernooijet al. (29), an 18% reduction in mortality was found in patients in specialized hospitals, compared to patients in general hospitals (HR adjusted for age and stage: 0.8 (95% CI 0.7–1.0). In addition, Mirjam et al. found that the risk of dying for women who did not undergo the surgical treatment by SOs according to guidelines was almost twice higher than the risk for those who underwent surgery according to the guidelines (1). Other findings in the two studies have shown a 25% reduction in the death rate in women diagnosed with advanced ovarian cancer and seen by SOs compared to women seen by other surgeons (19, 41).

In a study by Paulsen et al., the mortality rate was lower for patients operated on in specialized centers compared to other hospitals (HR ¼ 1.81). Besides, the chance of receiving optimal chemotherapy was lower among patients treated in non-teaching hospitals (OR ¼ 0.24) (37).

In fact, according to Chan et al. (36), the 5-year disease-specific survival of patients who did not undergo primary surgery by a SOs and did not receive chemotherapy was of 7.1% in contrast with 41.0% in those who received multimodality treatment when seen by SOs (P.001).

However, others (22, 32) have not considered the treatment provided by a SO an independent prognostic factor for improved survival for all stage divisions. There was no significant survival difference between patients operated on by SOs and those operated on by general gynecologists.

Table 1. Cytoreductive surgery outcomes and mean survival

Authors	Cytoreductive surgery outcomes		Mean survival	
	SO	Gynecologists	SO	Gynecologists
Engelen et al. (1)	62%	45%	54%	45%
Aletti et al. (26)	nm	Nm		
Eisenkop et al. (20)	81.7%	37.8%		
Olaitan et al. (27)	2.06 *>			
Bailey et al. (28)	nm	Nm		
Junor et al. (19)	nm	Nm	6-9 months >	
Vernoojii et al. (29)	57%	37%		
Marth et al. (3)	27%	11%	69%	61%
Kumplainen et al. (31)	nm	Nm		
Marx et al. (30)	nm	Nm		
Tingulstad et al. (18)	nm	Nm	21 months	12 months
Paulsen et al. (37)	nm	Nm	20% >	
Carney et al. (14)	nm	Nm	31.3%	

4. Morbidity

It has been shown that the residual tumor volume is one of the most important prognostic factors (16–18).

To achieve a complete cytoreduction, aggressive surgical techniques should be performed, including bowel resection and anastomosis, urologic procedures, diaphragm peritonectomy and upper abdominal resection (15).

Prior studies have established a direct relationship between surgical morbidity and the degree of cytoreduction (42). Eisenkop et al. (21) demonstrated that although women operated on by SOs had more extended hospital stays, more blood loss, transfusions and longer operative time, they had lower perioperative mortality of 2.4% compared to 9.5% in case of other surgeons [P = 0.02]. Similarly, the latter authors demonstrated that the presence of the SOs intraoperatively was associated with more perioperative morbidities and this was explained by the more complicated procedure performed by SOs.

In contrast, a shorter hospital stay and lower hospital-related costs of care in high-volume hospitals were recorded (11).

Also, a study by Birkmeyer et al. (39) included in the Surveillance Epidemiology and End Results, concluded to lower operative mortality in high-volume hospitals.

A retrospective study conducted in 2009 (43) had also shown that new surgical methods led to increased morbidity.

However, others have not found an increase in morbidity despite the aggressiveness of surgery (38, 44). On the other hand, some stated that there might be a bias in the selection of patients as those with comorbidities are more likely seen at central hospitals, while the healthier ones are examined in the general hospitals (37).

Discussion

OC is the most common cause of death in women out of all gynecologic cancers (1). The management of these women according to guidelines is necessary to improve the patients' outcomes (1). Surgical care according to guidelines is among the most important prognostic factors (45).

Several studies have noticed that SOs respect more operational guidelines than other surgeons in the treatment of OC (1). The care provided by experienced surgeons or by specialized centers seemed to be of a high standard, allowing an appropriate staging and an optimal debulking (24, 31). Thus, the Society of Gynecologic Oncologists and the American College of Obstetricians and Gynecologists (ACOG) (46) recommend the referral of patients with OC to SOs.

Over the past decades, the surgical management of patients with OC has included new complex techniques, such as intestinal resection, dissection of lymph nodes or diaphragm peritonectomy and partial liver resection.

Many authors demonstrated that a SO was more likely to determine the appropriate staging involving extensive surgical procedures (1, 3, 6–8). Consequently, this allows a better selection of the patients requiring adjuvant chemotherapy (19, 20, 38). Physicians working in cancer units were more experienced in the patients' selection (2).

Similarly, the number of unstaged or under-staged patients was more significant when operated on by other surgeons (12, n37), leading to under-treatment.

The main reasons for the inadequate staging are the lack of training and the maintenance of surgical skills of the general gynecologists (30, 31).

Several studies have reached the same conclusion, i.e. a SO was more likely to achieve complete cytoreduction than other specialists (1, 18–23, 25). In addition, specific surgical training is essential.

Moreover, the complete debulking was most frequently performed in large departments where a multidisciplinary team provided the treatment. Indeed, SOs were more likely to operate on at specialized hospitals (38).

The survival advantage was notable when patients were seen by SOs (11, 37, 38). Different studies concluded to a positive correlation between the specialization of the surgeon or the volume of patients in the hospitals and the survival of patients with OC (4, 5, 36, 37).

It has been suggested that the improvement of survival resulted from a more aggressive surgery providing a maximal cytoreduction (18, 47). Griffiths et al. (48) were the first to demonstrate an inverse relationship between the amount of residual tumor and the survival of patients with advanced disease.

In addition, several studies supported the fact that surgery conducted by SOs decreased the recurrence rate (6, 8, 25, 37).

Moreover, a reduction in the risk of dying in patients who underwent surgery by SOs was noticed (1, 38). In contrast, treatment by inexperienced surgeons increased the risks of recurrence and mortality (34). Thus, the centralization of the treatment of OC seems to be the key to optimizing the survival rates in patients with this disease.

Most importantly, the skills of SOs may depend on the number of OC operations performed, obtaining a dedicated learning curve required for the improvement and the maintenance of their skills (15, 30, 38).

Furthermore, a positive relationship between surgical morbidity and the degree of cytoreduction was shown (42). Patients operated on by SOs had more extended hospital stays, more blood loss, transfusions and longer operative time (21) since more complicated procedures were performed.

However, patients treated by a SO had lower perioperative mortality (21).

Different reasons could explain the lack of referral of those women to SOs, such as the difficulties of access to care, the lack of knowledge of the physician about adequate guidelines and the physician's financial gain. Furthermore, the public is poorly informed about SOs, and this may limit optimal management (40).

Therefore, further patient and physician education are necessary to assure that patients with OC are appropriately referred to SOs to improve the outcomes and the survival rate in case of this aggressive disease.

Conclusions

OC is the most lethal of all gynecologic malignancies. The current literature search concludes that the

specialization of the gynecologist as well as the hospital are correlated with appropriately staged and optimally cytoreductive surgery, leading to improved survival.

We assume that patients with an early and advanced stage of OC should be referred to SOs in specialized centers to ensure high-quality comprehensive care including surgery and chemotherapy.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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