

Diaphragmatic Surgery in Patients with
Advanced-Stage Ovarian Cancer: A
Literature ReviewOlivia Ionescu¹, Nicolae Bacalbasa^{2*}, Paris Ionescu³ and Irina Balescu⁴¹"Bucur" Maternity Hospital, Bucharest, Romania²"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania³"Ovidius" University, Faculty of Medicine, Constanta, Romania⁴"Ponderas" Hospital, Bucharest, Romania

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Abstract

Surgical management of advanced-stage ovarian cancer can require diaphragmatic surgery to achieve complete cytoreduction. If complete cytoreduction can be accomplished with the use of this procedure, it is conceivable that benefits in clinical outcomes may be offered to patients with aggressive, advanced ovarian cancer. Diaphragmatic surgery increases the rates of optimal primary debulking surgery and improves survival with an acceptable and manageable morbidity rate. The aim of this review is to evaluate the role of diaphragmatic debulking in the natural history of advanced-stage ovarian cancer and its survival benefit and the assessment of the relative post-operative complications.

Introduction

Ovarian cancer is a lethal malignancy for patients with advanced disease without any significant survival figures despite medical progresses [1]. Because of late diagnosis, the overall five-year survival rate for ovarian cancer is approximately 30%. Over 75% of the patients will be diagnosed with FIGO stage III or IV, with involvement of the upper abdomen. Metastases to the diaphragm, especially to the right hemi-diaphragm, are very common and up 40% of patients advanced-stage ovarian cancer have bulky metastatic diaphragmatic disease which leads to suboptimal cytoreduction and therefore to a lower rate of survival [2].

Retrospective and prospective reports have demonstrated that optimal cytoreduction for advanced-stage ovarian cancer is the cornerstone of effective treatment [3]. Surgical procedures aimed at treating diaphragm disease increase the rate of complete and optimal debulking and yield better survival compared to patients with residual disease found only in the diaphragm [4,5]. The reports about the experience with diaphragmatic surgery in advanced-stage ovarian cancer highlight feasibility, improvement in outcome in cases of optimalcy to reduction, and specific pulmonary morbidity [6,7]. Moreover, the performance of extensive abdominal procedures, such as partial liver section, distal pancreatectomy or splenectomy, may lead to improved cytoreduction, but increases the postoperative morbidity (digestive fistula, lymphocyst or infection) [8]. Therefore, radical surgery for advanced ovarian cancer could improve survival but with an increase in postoperative morbidity [9,10].

Depending on the extension of the disease, surgery of the diaphragm can include: ablation (argon beam coagulator), aspiration (cavitron ultrasonic surgical aspirator), peritonectomy ("stripping"), and full-thickness diaphragm resection. Even though these surgical procedures come with a potential price of increased intra- and post-operative morbidity- pulmonary and non-pulmonary complications such as (pleural effusion, fever or infection), they increase the rate of optimal cytoreduction and are related with improved survival rates in patients with advanced-stage ovarian cancer undergoing primary cytoreduction and interval debulking surgery) [11].

Diaphragmatic peritonectomy and full thickness diaphragmatic resection with pleurectomy at radical debulking in terms of surgical morbidity

Several studies have reported rates of pulmonary complications after peritonectomy and/or resection with pleurectomy for ovarian cancer. In these studies, the rates of diaphragmatic surgery ranged from 14 to 100%, and complete surgery was achieved in 43-93% of cases. Pneumothorax was found in 10-33% of cases and pleural effusion occurred in 10-59% of cases, depending on the rate of chest drainage established during surgery (from 0 to 65%) [12,13]. According to other study) [14], the most important and frequent complication is pleural effusion (42.5%). The elective placement of chest tubes in case of large diaphragmatic resections has been also reported [14-16]. This most likely reduces the occurrence of a pleural effusion as the pleura is drained [17,18]. Patients with

intra-operatively placed chest tubes feel subjectively better due to the absence of dyspnea and the tube can be removed faster (5-10 days) than in patients needing postoperative placement of a chest tube [16]. On the other hand, the need for secondary drainage or pleural puncture extends the length of hospitalization and increases the postoperative pain [14]. Rates of secondary pleural puncture or chest tube placement in the literature ranged from 0 to 44% and this variability may be related to the number of chest drains inserted during surgery [19,20].

In order to prevent pulmonary complication, the relatively low rate of thoracentesis or pleural drainage actually does not support the routine use of prophylactic chest tube placement and even if Chereau, et al. [15] reported the use of this procedure in anticipation of pleural opening, the authors conclude that this approach still needs further evaluation. The intra-operative placement of a chest tube could be considered in patients undergoing complete liver mobilization and large diaphragmatic peritoneal or full thickness resection [21].

Risk factors for the occurrence of pulmonary complications are the addition of other upper abdominal procedures and the size of the diaphragmatic excision. A multivariate analysis conducted by Eisenhauer and coworkers [14] showed that pleural effusion was statistically well predicted only by hepatic mobilization, although this procedure still represents a crucial step to perform a safe and complete surgery in the diaphragmatic region. There is a strictly linkage between liver mobilization and postoperative pleural effusion (52.3% vs. 16%; $p < 0.0027$) and, moreover, a direct correlation between the size of the diaphragmatic resection and the risk of post-operative pleural effusion (54.1% vs. 23.5%; $p < 0.034$). These results support the literature data [22,23] demonstrating that pulmonary complications represents the main morbidity of diaphragmatic surgery and suggest that the respiratory status of patients with diaphragmatic perforation is the main parameter that requires maximum attention in the post-operative period in order to avert dyspnea [23].

Aim of diaphragmatic surgery in initial surgery and interval debulking surgery and impact on survival

In recent years, several efforts have been made to underline the role of diaphragmatic debulking and its survival advantages [23,24]. These studies have demonstrated that diaphragmatic metastases can be resected with various surgical techniques- argon beam coagulator, peritonectomy or muscle resection- depending on the surgeon's ability to accurately determine the type and the extension of the disease. The deep knowledge of the upper abdominal anatomy and of the liver mobilization manoeuvres are fundamental to allow radical exploration and debulking of the diaphragm, limiting the risk of major vessels injuries (retro-hepatic caval vein, hepatic ilus, supra-hepatic veins, diaphragmatic vessels) with severe haemorrhage [25].

Although in chemotherapy-treated patients the de-peritonealization of the diaphragm is more difficult with a trend to more bleeding and increased risk of pleural accidental damage, there are no differences in terms of type of diaphragmatic debulking and morbidity rates according to different indications to surgery [23]. The European Organization for Research and Treatment of Cancer performed a randomized trial [26] which compares initial surgery in 329 patients with interval debulking surgery after pre-operative neoadjuvant chemotherapy in 339 patients with stage IIIC and IV ovarian cancer. Mortality in the group with initial surgery

was considerably higher than in the group who received interval debulking surgery (2.7% vs 0.6%) and a similar result has been obtained for morbidity with a higher digestive fistula rate in the group with initial surgery (1.2% vs 0.3%) [27]. This trial shows that in 95% of cases a complete cytoreduction can be obtained either at the time of initial surgery or interval debulking surgery with a rate of pleural effusion and pneumothorax requiring drainage of 5% [26,28]. Optimal RD after surgery is correlated with a better prognosis in patients undergoing interval debulking surgery [8,29]. Each decrease of 10% in residual tumor volume is followed by an increase of 5.5% in median survival in advanced ovarian cancer patients undergoing primary cytoreduction [6]. In the same direction, the proportion of patients undergoing complete cytoreductive surgery is independently associated with overall post-recurrence survival time [30]

G.D. Aletti, et al found a survival advantage for treatment of diaphragm disease when considering either all patients with diaphragm disease (53% vs.15%) or only the subset with diaphragm disease who underwent optimal cytoreduction (55% vs. 28%). For the subgroup of patients with advanced cancer and diaphragm involvement, there is a prognostic advantage for patients debulked to no macroscopic tumor compared to patients who have residual disease between 0 and 1 cm [11]. The specific removal of diaphragm disease in advanced-stage ovarian cancer is superior to leaving disease, even within the subcategory of "optimally debulked" patients with both stage III and stage IV disease [3].

Conclusion

Diaphragmatic surgery is an essential step in cytoreductive surgery of advanced-stage ovarian cancer and improves survival. If this surgery is used, it can cause pulmonary complications in addition to its related- morbidity rate due to the need for radical surgery. Although the use of diaphragmatic peritonectomies and full-thickness resections has to be modulated by the type of disease, both procedures are often required and the expertise should be available when attempting cytoreductive surgery with the aim of no residual disease. There are no differences in terms of type of diaphragmatic debulking and morbidity rates according to different indications to surgery.

The published literature about the association between the degree of residual disease and survival demonstrates that less residual disease correlates with a better survival and that a better survival rate is associated with no gross residual disease. As the goal of cytoreductive surgery is the removal of as much grossly evident disease as it is feasible and safe for the patient, the role of diaphragmatic resection in the pursuit of complete cytoreduction with the aim of improving disease-free survival is supported.

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