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12. The role of video-assisted thoracic surgery (VATS) and intrathoracic cytoreductive surgery in gynecologic malignancies

John P. Diaz and Dennis S. Chi

*Gynecology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center
New York, NY, USA*

Ovarian cancer is the second most common gynecologic malignancy in the United States, affecting 1 in 70 American women. Most women present with advanced-stage disease, which is why ovarian cancer is the most lethal gynecologic malignancy, with an estimated 15,520 deaths in 2008 [1]. While fallopian tube and primary peritoneal cancers are rare malignancies, they are histologically similar to ovarian cancer and are approached using the same treatment strategies.

Primary surgical debulking is a fundamental component of ovarian cancer treatment in the majority of patients with advanced-stage disease at initial presentation. While the definition of optimal debulking has ranged from complete gross resection to ≤ 2 cm, studies have consistently demonstrated that optimal vs. suboptimal debulking is associated with improved overall survival [2-10]. Even among the subset of patients with stage IV disease as evident by malignant pleural effusion,

Correspondence/Reprint request: Dr. Dennis S. Chi, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue
New York, NY 10065, USA. E-mail: gynbreast@mskcc.org

intraparenchymal liver metastasis, or other extraperitoneal disease, several authors have reported survival benefits when optimal cytoreduction can be achieved [3, 11-18].

It is estimated that more than one third of patients with stage IV ovarian carcinoma present with pleural effusions [18, 19]. Many patients with malignant pleural effusions are evaluated with a computed tomography (CT) scan to determine whether bulky thoracic disease precludes an attempt at abdominal surgical cytoreduction. It is unclear whether an accurate assessment of intrathoracic disease and extent of diaphragmatic pleural involvement can be made from radiographic studies alone. The presence of macroscopic intrathoracic disease may alter patient management, particularly if unresected > 1-2 cm intrathoracic tumor deposits would leave the patient with suboptimal residual disease at the conclusion of maximal intra-abdominal cytoreduction.

At presentation, stage IV disease is diagnosed in approximately 10% of patients with epithelial ovarian cancer [20]. The role of cytoreductive surgery in this group continues to be debated. Goodman et al. described the role of cytoreductive surgery in the management of stage IV disease. In their initial series evaluating primary and interval debulking in 35 patients with stage IV disease, they reported no difference in survival among patients who had optimal intra-abdominal cytoreduction [21]. Since this early report, several authors have reported improved survival in association with optimal primary debulking (Table 1 [3, 11-15, 17-19, 21]). Among the subgroup of patients classified as having stage IV disease based on malignant pleural effusions alone, the reported rates of optimal primary debulking range from 27-78% [11-14, 16-18].

The benefits of debulking in patients with malignant pleural effusions compared to patients with other stage IV disease criteria have been evaluated, with mixed results. In a study of 84 patients with stage IV disease, including 32 (38%) of 84 patients with malignant pleural effusions, Bristow et al. reported a median survival of 38.4 months in optimally debulked patients (≤ 1 cm) and 10.3 months in suboptimally debulked patients ($P=0.0004$). On univariate analysis, there was no difference in median survival comparing patients with pleural effusion and other stage IV criteria. Munkarah et al. studied 108 women with stage IV ovarian carcinoma. The median survival of the optimally debulked patients was 25 months versus 15 months for the suboptimally debulked patients ($P<0.02$). However, there was no statistical difference in median progression-free survival between the two groups. Interestingly, when they compared patients with pleural effusions only to other stage IV patients, they found no difference in survival between optimally debulked patients (median, 25 months) compared to suboptimally (defined as < 2 cm) debulked patients (median, 23 months) ($P=0.7$) [15]. In contrast, among a

Table 1. Cytoreductive surgery in patients with stage IV ovarian carcinoma.

<i>Study</i>	<i>Year</i>	<i>No. of patients</i>	<i>Optimal cytoreduction</i>	<i>Survival advantage for optimal debulking</i>
Goodman et al. [21]	1992	35	2 cm	no
Liu et al. [14]	1997	47	2 cm	yes
Curtin et al. [13]	1997	97	2 cm	yes
Munkarah et al. [15]	1997	100	2 cm	yes
Bristow et al. [3]	1999	84	1 cm	yes
Bonnefoi et al. [19]	1999	169	2 cm	no
Naik et al. [17]	2000	37	2 cm	yes
Akahira et al. [18]	2001	225	2 cm	yes
Brunisholz et al. [12]	2005	23	2 cm	no
Aletti et al. [11]	2006	50	1 cm	yes

smaller cohort of 23 patients with stage IV disease, Brunisholz found that 9 patients with pleural effusions had reduced survival compared with that of patients with other sites of distant metastasis [12].

Although several retrospective reviews have demonstrated a survival benefit to optimal intra-abdominal debulking in patients with malignant pleural effusions, these patients still have decreased survival when compared with patients who have disease confined to the abdomen. Eitan et al. compared the survival of optimally cytoreduced stage IIIC and stage IV patients by pleural effusion criteria. The median survival of the optimally cytoreduced stage IIIC patients was 58 months compared to 30 months for the stage IV patients ($P=0.0016$) [22]. While the poorer prognosis likely reflects the more aggressive and advanced nature of disease, which extends extraperitoneally, the authors of this prior report from our institution also raised the question of whether undetected bulky residual intrathoracic disease contributed to this difference.

Juretzka et al. reported our experience with video-assisted thoracic surgery (VATS) before planned abdominal exploration in 23 patients with moderate to large pleural effusions and advanced ovarian, fallopian tube, primary peritoneal, or other cancers [23]. VATS was performed for right-sided effusions in 17 patients (74%), and a median of 1350 mL (range, 400-3700 mL) of pleural fluid was drained. VATS demonstrated macroscopic disease in 15 patients (65%), with nodules > 1 cm in 11 (73%) of 15 and nodules < 1 cm in 4 (27%) of 15.

Macroscopic intrathoracic disease was found in 4 (40%) of 10 patients with negative cytology. Intrathoracic cytoreduction was performed in 3 (27%) of 11 patients with intrathoracic disease < 1 cm. After VATS, 12 (52%) of 23 patients underwent primary surgical management, with cytoreduction to ≤ 1 cm achieved in 11 (92%) of 12 patients. The other 11 patients received primary chemotherapy after undergoing diagnostic laparoscopy alone (4/11) or no further abdominal exploration (7/11). Nine of these patients proceeded to interval cytoreduction, while 2 had pathology demonstrating upper gastrointestinal and lymphoma primaries at the time of VATS. Final diagnosis of primary site of disease included the following: ovary, 14 (61%); endometrial, 2 (9%); dual ovarian/endometrial primaries, 1 (4%); fallopian tube, 1 (4%); primary peritoneal, 1 (4%); and other, 4 (17%). Overall, findings at VATS altered primary surgical management in 11 (48%) of 23 patients.

An update of our initial experience examined the primary management and oncologic outcomes of these patients [24]. In this review, 40 patients with advanced ovarian carcinoma and pleural effusions underwent VATS. The primary management of 16 (40%) of these patients was altered based on the findings at the time of VATS. Patients who after VATS were directed to neoadjuvant chemotherapy instead of primary surgical cytoreduction because of findings of pleural disease had a 2-year progression-free survival rate of 17% compared to 40% for the primary cytoreductive group. The improved progression-free survival for the primary cytoreduction group compared to the neoadjuvant group did not reach statistical significance ($P=0.10$), perhaps related to our small sample size (Figure 1).

The role of cytoreductive surgery in advanced ovarian carcinoma followed by platinum-based chemotherapy has been well established. The goal of cytoreductive surgery is to obtain an optimally debulked status, with no residual tumor > 1 cm. Patients who present with pleural effusions should be evaluated for the presence of malignant pleural effusions and intrathoracic disease > 1 cm. CT scans have been utilized to assess for intrathoracic disease; however, there have been no randomized trials to evaluate their sensitivity or specificity. We can infer from the inability of these scans to accurately predict which patient will have an optimal abdominal debulking that their utility intrathoracically would be similar [11]. As such, we believe that patients who present with suspected advanced ovarian carcinoma and pleural effusions should be assessed with a VATS procedure. The VATS procedure will not only allow for an accurate assessment of intrathoracic disease but provide for an attempt at intrathoracic debulking, if necessary. Furthermore, VATS provides the opportunity to appropriately triage patients to neoadjuvant chemotherapy who may have otherwise undergone an abdominal cytoreductive procedure that may not have benefitted her due to unknown bulky intrathoracic disease. The suggested treatment paradigm is outlined in Figure 2.

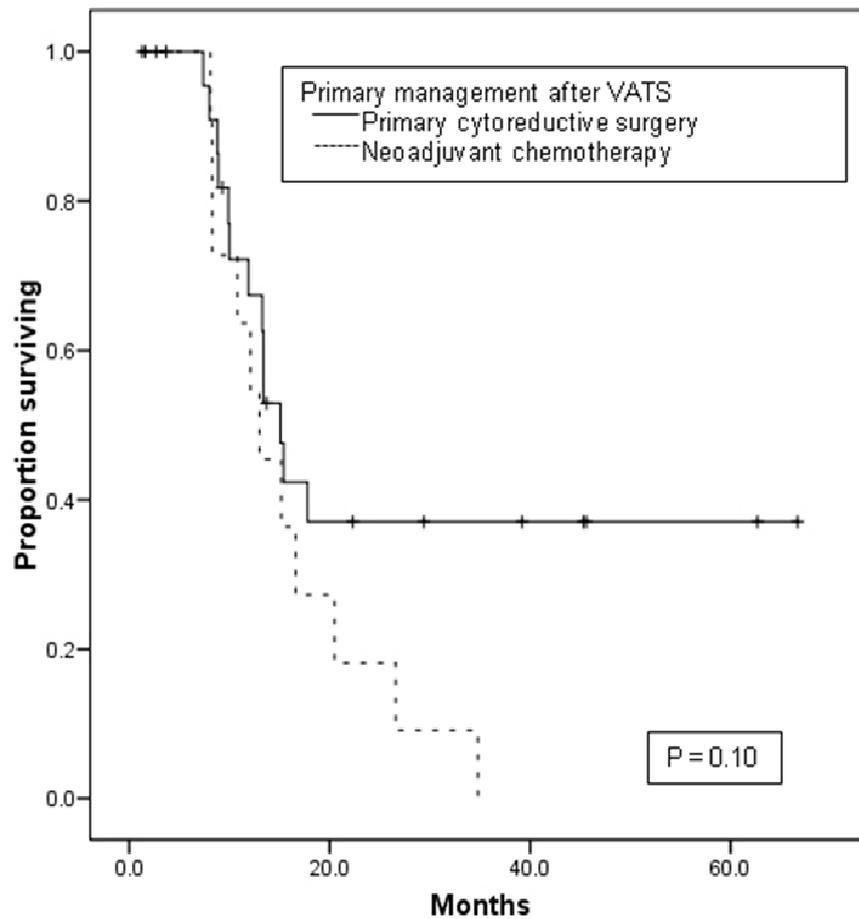


Figure 1. Progression-free survival after VATS.

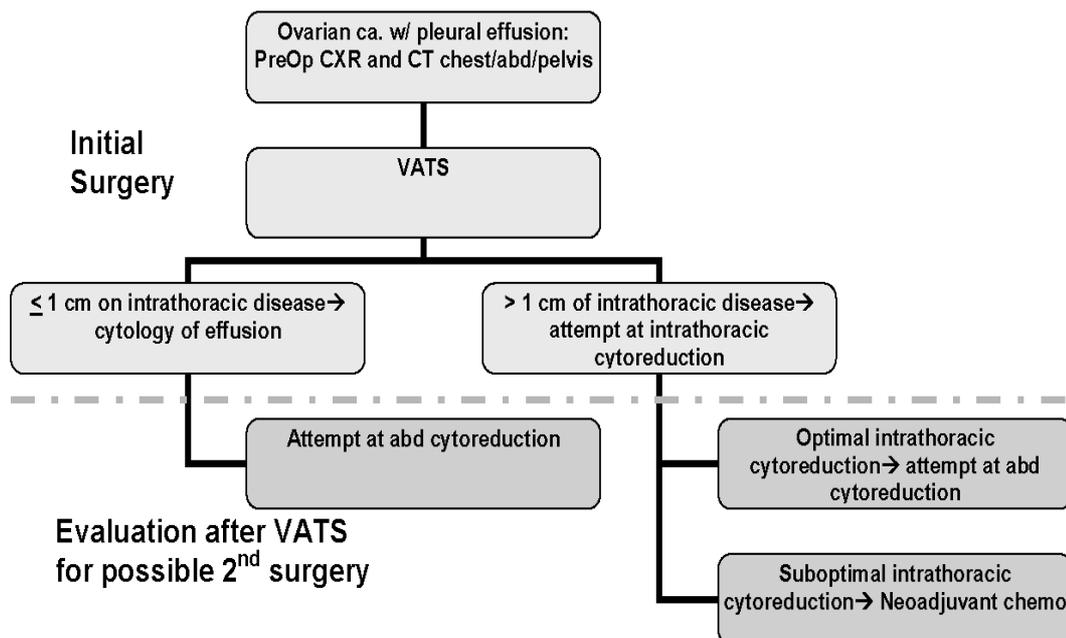


Figure 2. Management of suspected advanced ovarian carcinoma with pleural effusions.

The VATS procedure

Indications to perform a VATS procedure for gynecologic malignancies include the following:

1. Diagnosis of macroscopic intrathoracic malignant disease when pleural effusion is found in a patient with advanced mullerian malignancy (Figure 3)
2. Treatment of malignant pleural effusion
3. Resection of intrathoracic bulky disease and/or ablation of pleural-based disease in the setting of the maximal debulking effort
4. Assessment of full-thickness diaphragmatic involvement



Figure 3. Upright chest radiograph: Patients with a suspected advanced ovarian malignancy who have moderate to large pleural effusions on an upright chest radiograph should undergo a video-assisted thoracic surgery to evaluate the intrathoracic cavity for macroscopic disease prior to an attempt at an intra-abdominal cytoreductive surgery. Moderate to large pleural effusions are defined as effusions on an upright chest radiograph in which layering fluid occupies 1/3 or greater of the pleural cavity, as seen above.

Relative contraindications for VATS include the following:

1. No intra-abdominal surgical effort is planned, except when treating malignant pleural effusion
2. Ventilator dependency
3. Noncompliant lung
4. Severe emphysema
5. Chest wall involvement by tumor
6. Small thoracic cavity or significant anatomic restrictions
7. Hemodynamic instability
8. Coagulopathy

An anesthetic team experienced in thoracic procedures is important, as VATS cannot be performed without unilateral pulmonary atelectasis. Intubation is preferably performed with a double-lumen tube that allows one-lung ventilation and ensures collapse of the chosen lung.

For a diagnostic procedure without a difficult resection, a single surgeon can hold the camera and possibly the biopsy forceps, and one monitor may suffice. If two surgeons are needed, two monitors are placed on either side of the patient's head, providing the best views for both members of the operating team [25, 26].

The patient is placed in the lateral decubitus position as for conventional thoracotomy. To ensure maximal stretching of the intercostal spaces and to avoid obstruction to camera movement, the operating room table is slanted downward on both sides of the center so as to lower the pelvis and head (Figure 4).



Figure 4. Patient in the lateral decubitus position.



Figure 5. The incision for the first trocar is placed along the mid-axillary line in the sixth intercostal space.

The first trocar is meant for the camera, as in laparoscopy. A 10-mm or 5-mm trocar can be used depending on availability and operator preference. The first trocar is placed along the mid-axillary line in the sixth intercostal space (Figure 5). This location provides an excellent view of all pleural spaces, the lung parenchyma, and the mediastinum. The skin incision is made parallel and above the seventh rib. A small clamp is introduced through the intercostal muscles and pleura above the rib to avoid the intercostal vessels and neurovascular bundle that run below each rib. The clamp is opened, widening the intercostal space. Some surgeons advocate the direct digital exploration of the pleural cavity beneath the incision. The first trocar is then inserted, again avoiding the blood vessels running inferior to the rib.

If pleural effusion is present, it is drained through the trocar and sent for cytology. The 10- or 5-mm camera is inserted, and video-assisted exploration of the pleural cavity is performed (Figure 6). Operative ports may now be positioned, if needed. The operative ports are usually put along the anterior and posterior axillary line between the fourth and sixth intercostal spaces. Some surgeons advocate performing the anterior skin incision under the mammary fold to improve the cosmetic result. If malignant lesions are found, they can be biopsied or resected. Care should be taken to avoid seeding of tumor cells during extraction of tissue from the chest. A plastic endobag should be used for the larger specimens.



Figure 6. Exploration of the pleural cavity and biopsy of suspicious lesions.

Pleural disease can be ablated or resected as peritoneal disease is treated in the abdomen. This can be accomplished using the argon beam coagulator and monopolar electrocautery. Loculations of pleural effusion can be entered and drained.

All of the instruments that might be needed for an emergency thoracotomy must be ready in the operating room, and the staff should be ready for a conversion, if needed. At the end of the procedure, the trocars are removed and the lung is inflated. A chest drainage tube may be placed in the pleural cavity through one of the ports of entry to treat pneumothorax and drain pleural effusion in the postoperative period. All other ports are closed in layers to ensure air-tight closure.

Postoperative management

Patients are followed postoperatively with daily chest radiographs to ensure that the pneumothorax is not enlarging and that the chest tube is positioned properly without kinking. In cases of malignant pleural effusions, pleurodesis can be performed with talc or doxycycline. When the pleural

drainage is less than 200-300 cc per day, the chest tube can be removed at the bedside, making sure the incision is closed immediately after tube removal.

Complications of VATS are similar to those of conventional thoracotomy, such as air leak, postoperative bleeding, wound infections, empyema, and, in rare cases, respiratory failure [27]. Some of the less common complications include pneumonia, atelectasis, arrhythmias, and deep vein thrombosis. Pulmonary edema is not reported as a VATS-specific complication but is known to be related to pneumonectomies and lobectomies. Fluid overload should be avoided, and any acute respiratory complaint in the first 24-48 hours postoperatively should be worked up thoroughly.

There are, however, complications related to VATS and specifically to the insertion of the thoracoscopy ports. These complications include intercostal neuritis and port site metastasis of tumor.

Port-related complications can be minimized by good surgical technique, and pain can be decreased substantially [26]. Blunt-tip ports designed for thoracoscopy should be used, and the port should be introduced without force and under control. Some surgeons advocate making the skin incision directly over the intercostal space, avoiding oblique access. Excessive spreading of intercostal tissue should be avoided. A retrieval device will minimize the chances of port-site recurrence.

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