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Article

The role of video-assisted thoracoscopic surgery in patients with advanced ovarian malignancies: A prospective cohort study

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Abstract. *Background:* Through video-assisted thoracoscopic surgery (VATS), physicians can perform pleural effusion drainage in addition to evaluating macroscopic pleural disease and, in certain cases, removing large tumors. When compared to the chest CT , VATS can change the therapeutic plan of ovarian cancer patients and enhance FIGO staging accuracy. The key aim of this study is to inspect the accuracy of preoperative chest CT scans and the relevance of VATS in the decision-making process for patients with advanced ovarian cancer. *Methods:* This prospective study was conducted during the period between June 2021 and January 2023. Patients with advanced ovarian cancer (Stage III OR IV) were enrolled in the study and believed qualified to obtain the VATS. Preoperative evaluation of supra-diaphragmatic disease by Chest-CT was equated with the intra-operative VATS estimation to consider the function of VATS in further treatment choices in those patients. *Results:* There was a statistically meaningful variation between chest CT and VATS in detection rate of pleural nodules in advanced stage ovarian cancer patients. 8.8 % (6) of cases displayed suspicious nodules by chest CT, whereas pleural nodules were found in 29.4% (20) of cases

during VATS. It changed disease stage in 32.4% (22) of patients. Overall, VATS changed preliminary management decision based on clinical and radiological preoperative assessment in 18 patients constituting 26.5% of cases enrolled in our study. *Conclusion:* When ovarian cancer is assumed to be advanced, VATS can be used to define the amount of the disease, obtain tissue for histopathologic diagnosis if macroscopic disease is found, treat the effusion, and choose patients for intrathoracic cytoreduction or neoadjuvant chemotherapy quickly and safely. Furthermore, VATS is more effective than chest CT in detecting intrathoracic disease.

Keywords: Video-assisted; Ovarian cancer; Stage III, IV; VATS; CT staging; Malignancy.

Introduction

The fifth most prevalent basis of mortality for women globally is ovarian cancer, the seventh most common disease overall. Ovarian cancer affects more than 225,000 women worldwide each year, with a lifetime risk of 1:50. (1) Approximately 70% of epithelial ovarian cancer patients have an advanced illness when they are first diagnosed, necessitating cytoreductive surgery and chemotherapy to maximize their chances of long-term survival. (2) There is strong evidence that individuals with primary advanced ovarian cancer (FIGO III and IV) should have the most aggressive surgical procedure possible. The proportion of supreme cytoreduction and lengthy median survival time were shown to be statistically significantly positively correlated in a meta-analysis of 6885 patients with stage III or IV ovarian cancer (3), and extended survival was related to the elimination of all visible macroscopic illnesses. (4)

The presence of macroscopic pleural disease may modify treatment decisions and significantly impair survival, especially if undiscovered and unresectable after initial debulking surgery. (5,6) When receiving an initial diagnosis for advanced ovarian cancer, a considerable percentage of patients (30–48%) exhibit signs of a pleural effusion (7), and this has been linked to lower overall survival rates. (8, 9)

In the past, most pleural effusion patients underwent a preoperative chest computed tomography (CT) scan to rule out the presence of bulky intrathoracic disease, which would prevent PDS from being attempted. (10) However, it has been questioned whether chest-CT is useful in evaluating pleural and supradiaphragmatic lesions in ovarian cancer patients. (11) According to certain studies, Chest-CT had a lower sensitivity (14%) and specificity (25%) for detecting macroscopic pleural illness in persons with developed ovarian cancer. (11,12) As a result, it is uncertain how many ovarian cancer patients have supra-diaphragmatic illness, and Chest-CTs may not be the best performing method for this kind of disease. (13)

Through video-assisted thoracoscopic surgery (VATS), doctors can perform pleural effusion drainage in addition to evaluating macroscopic pleural disease (14) and, in certain cases, removing gross tumors. (9) A small number of studies showed that VATS influenced the therapeutic management of ovarian cancer patients, resulting in an up- or down-stage as compared to the CT, enhancing FIGO staging accuracy.

(1,13) Additionally, a recent retrospective analysis discovered that patients who had the best outcomes had initial debulking surgery and had no macroscopic disease at VATS. (10)
The aim of the study was to evaluate the role of VATS in subsequent treatment decisions in these patients with advanced ovarian cancer, and to assess the validity parameters of preoperative chest CT scans taken the findings during VATS as the "true" diagnostic tool for supra-diaphragmatic disease in these patients.

Patients and methods

This prospective cohort study was performed in harmony with the Declaration of Helsinki at the gyneoncology department of El-Shatby Maternity University Hospital. Between June 2021 and January 2023, 68 patients with advanced ovarian cancer, FIGO stage III/IV, with or without pleural effusion were included in this study. Patients who were unsuited for single lung ventilation, had undergone prior lung surgery, had intrapleural adhesions, had pulmonary resection, or had previously been treated for ovarian illness were excluded.
All the included patients underwent a thorough preoperative evaluation, which included a history review, physical examination, gynecologic ultrasound to determine the adenxial mass's malignant status, and preoperative CT scans of the chest, abdomen, and pelvis to look for liver metastases, lung metastases, lymph node affection, ascites, and tumor markers.
Based on the preoperative CT-Chest scan, patients with advanced ovarian cancer (Stage III or IV) were deemed suitable for the VATS. To assist the breathing process under general anesthesia, medical comorbidities were calmed, and in the case of pleural effusions, pleural drainage through thoracocentesis or pigtail catheter insertion was performed preoperatively. All patients received an explanation of the procedure's nature and its risks. All patients signed informed written consents. Thoracic surgeons worked with Alexandria University Hospital's Department of Cardio-Thoracic Surgery to complete the procedure. For cytology, pleural fluids were collected. The pleural cavity was explored, and the diaphragm, lung, and pleural cavity were all examined. Any suspect locations underwent biopsies. Excised suspected nodules were examined pathologically. In the case of metastatic nodules, pleural excision was carried out, if practicable.

Surgical technique

A double-lumen tube was used to produce the usual anesthesia while the patient was in the lateral decubitus position. Through a 1.5-cm skin incision , a Kelly forceps was then introduced through it to carefully open wide the subcutaneous tissue and the muscle until it reached the parietal pleura. This procedure enabled a tiny quantity of air to enter the pleural cavity, which allowed for the safe insertion of the

first port (10 mm). The technique started with the placement of a 10-mm port in the sixth or seventh intercostal space. Through this site, the telescope (0° and 30°) for exploring the lung and the pleural cavity was introduced. Two additional ports were often inserted under endoscopic guidance: one anterior port in the 4th or 5th intercostal space in the anterior axillary line, and one posterior port in the 5th or 6th intercostal space in the posterior axillary line. One or two chest tubes were placed in the pleural cavity *via* the port incisions following a pleural lavage at the end of the process; these were withdrawn when the air outflow stopped, and the fluid level was less than 100 cc/day (Figure 1).

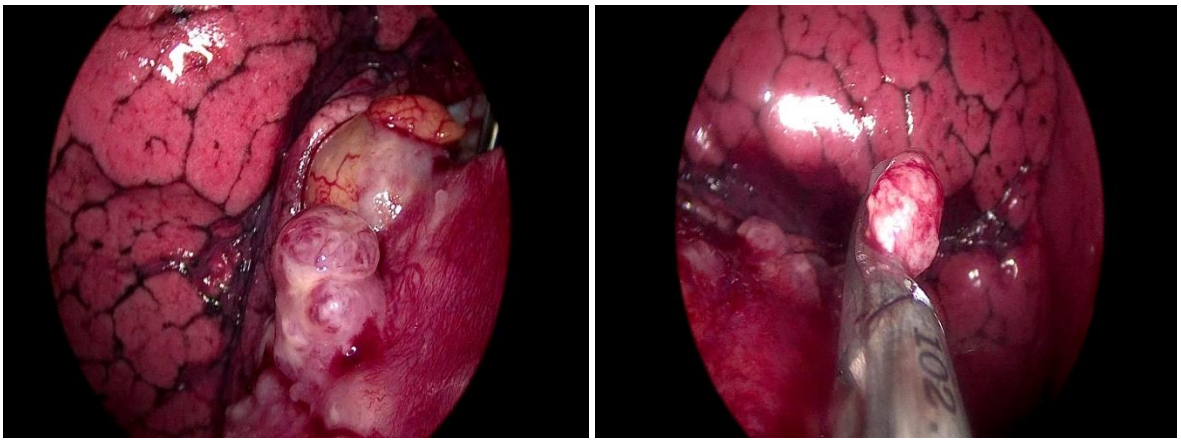

Figure (1) obtained during video-assisted thoracoscopic surgery showing pleural nodules of different sizes on parietal pleura of diaphragmatic surface and taking biobsy from pleural nodules.

Postoperative data

Preoperative evaluation of supra-diaphragmatic disease by Chest-CT was equated with the intra-operative VATS estimation to evaluate the function of VATS in further treatment assessments in those patients. Depending on the findings during VATS, patients were labeled into two groups:

(1) Group A: Patients who have taken neoadjuvant chemotherapy.
(2) Group B: Patients who underwent surgery for debulking. When VATS revealed no intrathoracic tumor or when total excision of tumor nodules was achieved during intraoperative frozen section histological evaluation, patients were deemed qualified for complete debulking.

Statistical analysis

With the assistance of the IBM SPSS software package ver., 20.0, data were supplied into the computer and estimated (IBM Corp., Armonk, NY). Numbers and percentages were utilized to illustrate qualitative data. The range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR) were

utilized to characterize quantitative data. For categorical variables, the chi-square test was employed to equal results among groups. When more than 20% of the cells have an anticipated count of less than 5, Fisher's exact or Monte Carlo is employed to adjust the chi-square statistic. To compare the two examined categories, the student t-test was utilized for normally distributed quantitative data. At the 5% level, the significance of the findings was verified.

Results

This study included 68 patients with advanced ovarian malignancies. There were no drop out of patients during the study. The mean age of patients was 52.29±9.84 years, 5.9% (4) were single and 94.1% (64) were married. According to menopausal status, 67.6% (46) of patients had menopause at the time of diagnosis. As regards BMI, the mean BMI of the study populace was 31.59±4.20 kg/m^2.
Tumor markers levels were investigated for studied cases. At presentation, the median CA125 was 517 U/mL. Median CA 19.9 was 6.35 U/mL and median CEA was 1.34 ng/mL. 85.3 % (58) of patients with FIGO III (2 with IIIa, 22 with IIIb, 34 with IIIC) and 14.7% (10) of patients with FIGO IV underwent VATS throughout the study. Final histopathological diagnosis of disease was done. Serous carcinoma constituted 76.5% (52) and poor differentiated grade of tumor was most common constituting 88.2% (60).

The median blood loss for VATS procedure was 20 ml and median volume of pleural fluid drained was 150 mL. Duration of VATS ranged from 30 to 90 min, with the median time was 45 min. Overall, VATS discovered macroscopic disease in 29.4% (20) of patients with nodules more than 1 cm in 7/20 patients (35%) and nodules less than 1 cm 13/20 patients (65%). As such, diseases more than 1 cm were discovered in 10.3% (7) of the total study group, while diseases less than 1cm accounted for an additional 19.1% (13). Pleural cytology attained preoperatively or at the time of VATS was positive in 33.8% (23) of patients, negative in 66.2% (45) of patients. Final histopathological diagnosis of malignancy was positive in 27.9% (19) of patients (Table 1). Regarding complications of VATS, we had 1 case of wound infection, 1 case of postoperative pneumothotax and 1 case of diaphragmatic injury with primary trochar insertion.

Table (1): Distribution of the analyzed cases corresponding to cytology and macroscopic disease during VATS (n = 68).

Parameter	n.	%
Cytology		
Negative for malignancy	45	66.2
Positive for malignancy	23	33.8
Nodules (n = 68)		
No	48	70.6
0.1-1 cm	13	19.1
>1.cm	7	10.3
Nodules site (n = 20)		
Right	6	30.0
Left	9	45.0
Bilateral	5	25.0
Pleural biopsy		
Negative	49	72.1
Positive	19	27.9

Comparing chest CT and VATS in detection rate of pleural nodules in advanced stage ovarian cancer patients. 8.8 % (6) of cases showed suspicious nodules by chest CT, whereas pleural nodules were found in 29.4% (20) during VATS. There was a statistically meaningful variance among both preoperative diagnostic modalities. (Table 2).

Table (2): Comparison between macroscopic disease in CT chest vs VATS (n = 68).

	Chest CT		VATS		^{McN}p
	N.	%	N.	%	
Nodules					
No	62	91.2	48	70.6	0.003*
Yes	6	8.8	20	29.4	

McN: McNemar test; **p:** p value for relating between CT and VATS; ***:** Statistically significant at $p \leq 0.05$

As shown in (Table 3), the only features correlated with malignant pleural effusion in cytology was the occurrence of any right-sided moderate or marked pleural effusion which was statistically significant. The size of left-sided pleural effusion (moderate or marked) and presence of moderate or marked ascites were significantly correlated with solid pleural metastasis. The incidence of pleural

effusion and detection of cardiophrenic lymph nodes on chest CT was significantly correlated with solid pleural metastasis and malignant pleural effusion cytology.

Table (3): Distribution of the considered cases corresponding to cytology and macroscopic disease during VATS based different parameters.

	Biopsy		⚜*	**p**	**Cytology**		⚜*	**P**
	Absent (n = 12)	**Present (n = 15)**			**Absent (n = 8)**	**Present (n = 19)**		
Any right marked or moderate effusion on chest CT								
Absent	8	10	0.000	FEp= 1.000	8	10	5.684*	0.026*
Present	4	5			0	9		
Any left marked or moderate effusion on chest CT								
Absent	9	7	2.217	FEp= 0.239	5	11	0.049	FEp= 1.000
Present	3	8			3	8		
	Biopsy		⚜*	**p**	**Cytology**		⚜*	**P**
	Absent (n = 49)	**Present (n = 19)**			**Absent (n = 45)**	**Present (n = 23)**		
Marked or Moderate ascites with any marked or moderate right effusion								
Absent	45	14	3.939	0.103	45	14	20.295*	FEp <0.001*
Present	4	5			0	9		
Marked or Moderate ascites with any marked or moderate left effusion								
Absent	46	11	13.073*	FEp= 0.001*	42	15	8.873*	FEp= 0.005*
Present	3	8			3	8		
	Biopsy		⚜*	**p**	**Cytology**		⚜*	**P**
	Absent (n = 49)	**Present (n = 19)**			**Absent (n = 45)**	**Present (n = 23)**		
Effusion + Cardiophrenic LNs								
Absent	45	11	10.853*	0.002*	41	15	7.022*	0.016*
Present	4	8			4	8		

χ^2: Chi square test; **FE:** Fisher Exact; **p:** p value for evaluating between absent and present; ***:** Statistically significant at $p \leq 0.05$

Considering diaphragmatic and pleural involvement on thoracic side by preoperative chest CT, VATS changed disease stage in 32.4% (22) of patients. This was attributed to both false-negative and false-positive cases detected by preoperative chest CT. As a result, VATS upstaged 29.4% (20) of patients, while downstaged 2.9% (2) of patients (Table 4).

Primary abdominal surgical debulking was done in 58.8% (40) of patients, while 41.2% (28) of patients extended on to take principal chemotherapy. Overall, VATS changed preliminary management decision based on clinical and radiological preoperative assessment in 18 patients constituting 26.5% of cases enrolled in our study (Table 4).

Table (4): Distribution of the calculated cases corresponding to VATS impact on disease staging & final decision.

VATS effect	N.	%
Up staged	20	29.4
Down staged	2	2.9
Equal staged	46	67.6
Final decision		
NeoadJuvant	28	41.2
Primary cytoreduction	40	58.8
Change of preliminary decision		
Not change	50	73.5
Change	18	26.5

Discussion

According to FIGO recommendations, the stage is assessed for patients with epithelial ovarian cancer and is regarded as the primary predictor of outcome. (15) While the mere existence of fluid in the pleural cavity is not considered a stage IV condition, malignant pleural effusion by cytology is. (15) In addition to stage, several additional prognostic markers have been discovered, containing age, the ascites , and how much disease is left behind after surgery. For both stages III and IV ovarian cancer, adequate initial cytoreduction has been shown to improve survival in several trials. (16, 17)

In general, stage IV patients with optimal cytoreduction have reported median survivals of 25 to 40 months, which is shorter than the 49 to 57 months observed for stage III patients with excellent cytoreduction. (18) In a trial of 84 patients with stage IV cancer, entering 32/84 (38%) with malignant pleural effusions, Bristow et al. found

that patients with optimally debulked disease (1 cm) had a median survival of 38.4 months, whereas those with residual disease had a median survival of 10.3 months (P = 0.0004). (19) Recent clinical trials have shown that the thorax is commonly engaged in advanced ovarian cancer, harboring pleural illness that is undiscovered at the time of diagnosis, and that this is probable to impair optimal debulking. (20 ,21)

At our institution, clinical practice is currently evolving. To find undetected intrathoracic disease and adjust patient therapy to achieve the greatest amount of cytoreduction, video-assisted thoracic surgery was done on patients with developed ovarian cancers. Here, 68 patients with advanced ovarian cancer, FIGO stage III/IV, with or without pleural effusion, were enrolled in the research and qualified to undergo VATS. We assessed the effectiveness of VATS in detecting intrathoracic illness in contrast to chest CT results, as well as its use in helping patients with developed ovarian cancer decide how to be managed.

Since our study was prospective and not dependent on retrospective data, we were able to prevent selection bias that may have impacted the outcomes. This was one of the shortcomings of several studies that were undertaken to assess the function of VATS in developed ovarian cancers. (10, 21, 22, 23) In these investigations, patients with VATS were suspected based on information from pleural cytology or CT results. We are the first study team, to our knowledge, to deploy VATS for patients with advanced ovarian cancers who do not have pleural effusions seen by chest CT and evaluate the effectiveness of VATS in these patients.

Overall, VATS in this investigation indicated macroscopic disease in 20/68 patients (29.4%), nodules bigger than 1 cm in 7 patients (35%), and less than 1 cm in 13 patients (65%), with nodules. We discovered macroscopic disease in 4/41 (9.8%) of advanced ovarian cancer patients without pleural effusion and 16/27 (59.3%) of patients with pleural effusion when comparing the detection of macroscopic disease in progressive ovarian cancer patients with or without pleural effusion. Once again, this is an advantage of our research because 40% of patients with pleural effusion will not receive the advantages of PDS if one thinks that all of them have macroscopic illness and should receive NACT or IDS. In contrast, if one assumes that all patients without pleural effusion don't have macroscopic disease and should undergo PDS, then approximately 10% of cases will have undiagnosed intrathoracic disease that will affect survival and will undergo extensive abdominal surgery to achieve optimal cytoreduction, but their overall survival will not be improved.

All patients with stage III or IV ovarian cancer and moderate or significant pleural effusion, according to Boerner et al. (10) had VATS. In 70% of patients, a macroscopic pleural illness was discovered. These findings are in line with our data analysis, which revealed that 11/15 (73%) of the patients with moderate or significant pleural effusion had macroscopic pleural disorder. In 65% of patients with moderate or significant pleural effusion who were investigated, Juretzka et al. (21) found macroscopic intrathoracic disease.

According to our study, preoperative chest CT showed pleural macroscopic disease in 6/68 (8.8%) of cases, whereas pleural nodules were discovered in 20/68 (29.4%) of cases during VATS. This difference in preoperative diagnostic modalities is statistically significant. Therefore, we view VATS as the benchmark. These outcomes are consistent with research by Mironov et al. (22) that discovered preoperative CT had a 14% sensitivity and 25% specificity for pleural status assessment. Additionally, they discovered that individuals with stages III or IV epithelial ovarian cancer had a worse prognosis when they had , moderate or large pleural effusions on their CT scans. According to Cohen-Mouly et al. (23), CT was only 14% sensitive and 25% certain for pleural condition. Only 2 of the 6 individuals who had pleural disease by VATS in a retrospective analysis of 12 patients with significant pleural effusion had chest CT identify pleural abnormalities. (24) Due to the poor chest CT performance, all these results favor the use of VATS.

Only the presence of any right-sided moderate or considerable pleural effusion, which is statistically significant, was related in our research to malignant pleural effusion in cytology. Moderate or pronounced ascites and the amount of left-side pleural effusion were strongly linked to the existence of solid pleural metastases. We discovered that CT characteristics typically thought to be indicative of solid pleural malignancy, for example solid pleural nodules, pleural thickening, and improvement, were not related with pleural malignancy at biopsies or cytology gained through VATS, which is in line with findings of a study comparing CT and VATS for the detection of thoracic metastasis (22).

Malignant pleural disease was linked in our research with the extent of the pleural effusion and the size of the ascites on CT. We discovered that solid pleural metastasis and malignant pleural effusion cytology were substantially correlated with the presence of pleural effusion and the identification of cardio- phrenic lymph nodes on chest computed tomography.

Operative time and morbidity were comparable to those seen in trials using VATS for other purposes. VATS, however, may have drawbacks. We had a case of post-operative pneumothorax, but since it was the first instance of the study with the cardio-thoracic surgery team's participation, it was determined that there was a lack of complete understanding of how to handle the chest tube under water seal. So, later, this difficulty was averted. We also had a case of unintentional trochar damage to the diaphragm during initial trochar insertion in a case of extensive ascites, which resulted in a rent of around 1 cm. The treatment was finished when the rent was sutured.

According to our findings, routine pleural cavity evaluation increased staging accuracy. As a result, VATS may influence therapy choices. VATS changed the treatment plan for 18/68 (26.5%) of the enrolled patients. Therefore, we advise VATS as the reference test prior to making a treatment choice for patients with stage III or IV ovarian cancer . In previous research, VATS was found to have an impact on treatment choices in 39% (23), 33% (27), and 41%. (25)

Our study has several limitations, including small sample size . Despite we had higher number of studied patients than most of studies on impact of VATS on management of cases with advanced malignancies .Only , a study conducted by Boerner et al.(10) was higher in studied population (100 patients) than ours but this was attributed to that their study covered a long period of time and was retrospective only for cases with moderate or large pleural effusion .The accuracy of CT in detecting intrathoracic disease was another limitation. Since many CT exams were carried out outside of our institutions, it may have been challenging to detect pleural metastasis on digitalized pictures from other institutions. Additionally, we did not assess VATS's potential therapeutic value.

However, it has been demonstrated that pleural involvement affects patients' prognosis. Combining extensive abdominal surgery with thoracic cytoreductive surgery has been considered. We've been criticized for not completing all the surgery and cytoreduction, if necessary, in the same session, but that was due to logistical issues with our institution.

Given this experience, VATS rather than chest CT alone is a more suitable staging technique. To examine the genuine diagnostic efficacy of VATS in patients with advanced ovarian cancers, more precise predictive values are required in a multicenter endeavor.

Conclusion

Our findings imply that VATS can be carried out quickly and safely in suitcases of suspected developed ovarian cancer to define the range of the ailment, obtain tissue for histopathologic diagnosis if macroscopic illness is found, treat the effusion, and choose patients for intrathoracic cytoreduction or a neoadjuvant chemotherapy tactic. Additionally, VATS is more effective than chest CT at detecting intrathoracic disease.

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Conflict of Interest: The authors declare that they have no competing interests.

Ethics Approval: Approval was obtained from the ethics committee of Faculty of medicine, Alexandria University in 2021. Approval number was 0201545.

Acknowledgements: Not applicable.

Consent to Participate: Informed consent was obtained from all participants included in the study.

Study Registration: NCT05840029.

https://clinicaltrials.gov/ct2/show/NCT05840029

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