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Mechanisms of Dissemination and Clinical Features of Thoracic Metastases in Ovarian Cancer: A Literature Review

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ABSTRACT

This literature review explores the mechanisms of thoracic dissemination in ovarian cancer and the clinical features associated with thoracic metastases. Ovarian cancer remains a leading cause of mortality among gynecologic malignancies, with nearly 75% of patients presenting with advanced-stage disease and high rates of recurrence despite surgery and chemotherapy. Most cases are diagnosed at late stages, contributing to poor survival outcomes and an increased risk of relapse. Common manifestations include small malignant pleural effusions, smooth pleural nodules, and metastatic lesions involving the lungs, pleura, or thoracic lymph nodes, which may mimic granulomatous disease. Recognizing these patterns is essential for accurate staging, guiding clinical decision-making, and assessing patient prognosis.

Keywords: ovarian cancer; thoracic metastasis; pleural effusion

INTRODUCTION

Thoracic metastases arising from gynecologic malignancies are frequently underdiagnosed and often underreported in clinical practice, largely due to low clinical suspicion and the limited use of advanced thoracic imaging techniques. Despite its clinical relevance, thoracic involvement in ovarian cancer is commonly overlooked because respiratory symptoms tend to be mild or nonspecific, and chest imaging is not routinely performed during initial evaluation [1].

Several studies have demonstrated that pleural effusion occurs in a substantial proportion of patients with advanced ovarian cancer, highlighting that thoracic extension is not uncommon in this population [2].

Importantly, thoracic involvement carries significant prognostic implications. Malignant pleural effusion has been consistently associated with reduced survival across various malignancies, including ovarian cancer [3]. Likewise, patients who develop pleural or pulmonary metastases exhibit poorer overall survival compared with those who have disease confined to the abdomen [4].

More recent work reinforces the clinical burden of thoracic metastasis. In patients presenting with moderate-to-large pleural effusion at initial diagnosis (clinical stage IVA), approximately 74% achieved effusion resolution after neoadjuvant chemotherapy. Yet, this group continued to represent a high-risk subset requiring careful clinical decision-making, highlighting the complexity of managing thoracic involvement even at first presentation [5].

Taken together, these findings underscore that thoracic involvement is both clinically meaningful and

prognostically relevant, warranting more systematic attention during initial assessment and ongoing management. To support this need, a structured understanding of thoracic dissemination and its clinical manifestations is essential. Therefore, this review aims to synthesize current evidence on mechanisms, epidemiology, clinical features, and management of thoracic metastases in ovarian cancer.

METHOD

This study was conducted as a narrative literature review that summarized current scientific evidence on the mechanisms of dissemination and clinical characteristics of thoracic metastasis in ovarian cancer. Relevant peer-reviewed studies and reviews describing pleural, pulmonary, and lymphatic involvement were examined, and key findings were synthesized to provide an updated overview of thoracic involvement in ovarian cancer.

RESULT

Mechanisms of Thoracic Dissemination

Ovarian cancer frequently disseminates throughout the peritoneal cavity, involving the omentum and even reaching hepatic or pulmonary parenchyma. The disease can spread through intraperitoneal, lymphatic, and hematogenous pathways. However, its dissemination is predominantly believed to occur via peritoneal circulation associated with malignant ascites formation rather than through the classical hematogenous metastatic route [6].

Malignant ascites (MA), characterized by the pathological accumulation of fluid within the peritoneal cavity, is a common manifestation of ovarian malignancy. MA is considered a hallmark of advanced-stage ovarian cancer, affecting more than one-third of patients across all epithelial subtypes, including serous carcinoma [7].

Thoracic metastasis may arise through hematogenous, lymphatic, or endobronchial routes [8]. The pulmonary system possesses several unique anatomical and physiological characteristics that increase its susceptibility to metastatic involvement. The lungs contain the densest capillary network in the human body, receive the entire cardiac output every minute, and serve as the primary reservoir for most lymphatic drainage entering the venous system [9].

Two major theories have been proposed regarding the timing of metastatic spread: late dissemination, in which metastasis occurs after genetic alterations in the primary tumor, and early dissemination, whereby single tumor cells are released early, remain dormant, and later initiate metastatic growth. Pulmonary metastasis requires an adequate blood supply, which may originate from the bronchial circulation, pulmonary circulation, or both. Although early concepts suggested that most pulmonary tumors received their blood supply predominantly from the bronchial circulation, more recent studies demonstrate that pulmonary neovascularization is common, with vascular patterns that are frequently complex and variable [9]. Overall, these mechanisms highlight the biologic heterogeneity of thoracic spread and help explain why thoracic involvement may present diversely across patients.

Clinical Manifestations and Diagnostic Evaluation

Symptoms resulting from pulmonary metastases may be either symptomatic or asymptomatic. Pulmonary metastases can present as solitary or multiple lesions, with a wide range of clinical manifestations. Some patients may be unaware of the presence of lung metastases, which are detected incidentally as pulmonary nodules. Systemic symptoms such as fatigue, nausea, anorexia, and weight loss are common. Meanwhile, local manifestations such as pleuritis or pleural effusion, often hemorrhagic in malignant neoplasms, are frequently observed [10]. Other symptoms may include cough, dyspnea, hemoptysis, and physical findings such as digital clubbing. Patients with pulmonary metastases may also exhibit signs of superior vena cava syndrome or characteristic features of a Pancoast tumor, such as Horner's syndrome.

In addition, general symptoms associated with metastatic cancer, such as vomiting, flank pain, loss of appetite, and shoulder pain, may also be present. On physical examination, pulmonary findings can range from normal to more specific signs, such as monophonic wheezing or decreased breath sounds [11].

Chest radiography and CT scans are the primary imaging modalities for evaluating thoracic metastases [8]. Radiologic imaging plays a central role in staging and monitoring patients with malignancies accompanied by pulmonary metastases. Chest X-ray remains the initial test for identifying lung metastases [12].

In patients with primary malignancies, the presence of multiple bilateral pulmonary nodules with radiologic features characteristic of metastases strongly indicates metastatic disease. It may eliminate the need for additional diagnostic procedures [13,14]. The size of pulmonary nodules typically ranges from 20 to 30 mm (50%), 10 to 20 mm (28.5%), and less than 10 mm (21.5%). Cavitating or necrotic nodules are present in 88.5% of cases and absent in 11.5% [11].

Epidemiology of Thoracic Involvement in Advanced Ovarian Cancer

Thoracic involvement in ovarian cancer, manifesting as pleural effusion, pleural implants, or pulmonary metastases, occurs variably depending on patient population, stage at diagnosis, and diagnostic methods. In a classic series of 357 patients treated at Yale–New Haven Hospital between 1966 and 1975, 169 (44.5%) had thoracic involvement, with pleural effusion present in 75% of those cases, and 12.3% showing solid pulmonary metastases [15].

However, more contemporary, population-based data indicate a lower prevalence: a study using the SEER Program database (serous ovarian cancer patients diagnosed 2010–2016) found lung metastases in 3.77% of 10,146 patients [16] Institutional data from a tertiary hospital in Indonesia (2014–2015) likewise reflect the rarity of thoracic metastases in clinical practice: of 292 ovarian cancer patients, only 5 had pleural metastasis and 7 had lung metastasis [17].

Clinical Impact and Definition of "Severe" Thoracic Disease

Thoracic metastases in ovarian cancer hold substantial clinical importance because they alter staging, guide treatment decisions, and strongly affect prognosis. In a retrospective study comparing chest CT with Video-Assisted Thoracic Surgery (VATS) among 44 patients with advanced epithelial ovarian cancer, pleural metastasis was confirmed in 26 patients (59%), and 74% of pleural effusions showed malignant cytology. Notably, only two CT features larger left-sided pleural effusion and presence of ascites were significantly associated with pleural metastasis, while typical imaging indicators such as pleural nodules or pleural thickening did not reliably predict malignancy [18].

In a broader cohort analysis, moderate-to-large pleural effusions in advanced ovarian carcinoma were associated with decreased overall survival compared with patients without macroscopic pleural disease; in a 100-patient VATS cohort, median overall survival was 44.5 months, but patients without macroscopic intrathoracic disease who underwent primary debulking surgery had a markedly higher survival (median OS 87.8 months) than those receiving neoadjuvant chemotherapy + interval debulking (median OS 37.4 months) [19] This emphasizes the prognostic significance of detecting macroscopic thoracic disease early in the clinical course.

In rare cases, isolated pulmonary metastases (without other distant spread) may be considered for surgical resection; however, data remain limited, and selection criteria are strict. In a multi-institutional series of 1,508 pulmonary resections for metastases from various primaries, only 6 (0.4%) involved ovarian cancer. Among them, when complete resection was achieved, and patients were carefully selected, some achieved mid- to long-term survival (disease-free or alive with disease at 38–61 months follow-up) [20].

Prognosis and Survival Outcomes

Studies have shown that tumors in the thoracic region occur in 44.5% of cases, and only 5.6% of these patients survive five years, compared with 49% of patients without evidence of thoracic involvement. Another study on patients with epithelial-type ovarian cancer reported that 38% had distant metastases, with a median survival of six months from the initial diagnosis of effusion. Among those with parenchymal lung metastases, 7.1% of patients had a median survival of eight months [11].

In patients undergoing pulmonary metastasectomy for gynecologic malignancies, thirty-seven individuals had isolated lung metastases (< three nodules). Twenty-three patients who underwent surgical resection were analyzed and compared with those who received chemotherapy alone. The median age at surgery was 56 years (range: 28–77 years). These patients included seven individuals with two or three pulmonary nodules and eight individuals with tumors unresponsive to chemotherapy. The cohort consisted of 14 patients with cervical cancer, who had a five-year overall survival (OS) rate of 61% after surgery; four patients with endometrial cancer, all of whom achieved a five-year OS of 100%; and five patients with ovarian cancer, all of whom also achieved a five-year OS of 100% following surgery [21]. These findings suggest that surgical intervention may offer meaningful benefit in highly selected cases, particularly when recurrence-free intervals are long.

Patients with a recurrence-free interval of more than two years after initial treatment demonstrated significantly better five-year survival outcomes. Among six patients who developed recurrent lung metastases, five underwent a second pulmonary metastasectomy, and all of them are currently alive with no evidence of disease. No serious complications occurred in the 29 surgeries performed. Although survival rates tended to be higher in the surgical group compared with the chemotherapy-only group, the difference was not statistically significant. Surgical removal of isolated lung metastases may offer favorable long-term outcomes with a low risk of complications, particularly in patients with a prolonged recurrence-free interval, tumors unresponsive to chemotherapy, or recurrent pulmonary metastases [21].

Management Implications

Management strategies depend on symptoms, extent of disease, and overall prognosis. For symptomatic malignant pleural effusion, individualized approaches (therapeutic thoracentesis, chemical pleurodesis, or indwelling pleural catheter insertion) should be selected based on lung re-expansion, estimated prognosis, patient preference, and local resources. Randomized and guideline-level data from MPE literature support these options across tumor types [22]. Systemic chemotherapy and, when appropriate, targeted maintenance therapies remain central for disseminated ovarian cancer; local thoracic interventions are complementary used to relieve symptoms or to render isolated disease resectable. Decisions regarding sequencing (e.g., neoadjuvant therapy to improve operability) should be individualized and coordinated by a multidisciplinary tumor board [23].

Consider pulmonary metastasectomy only for patients meeting strict selection criteria (controlled or controllable primary disease, limited nodal burden, adequate cardiorespiratory reserve, and informed patient preference), and discuss expected benefits and uncertainty due to retrospective evidence [24].

Early palliative involvement benefits patients with thoracic metastases by improving symptom control (dyspnea, pain, cachexia) and guiding goals-of-care conversations; use validated prognostic tools (e.g., PROMISE/LENT) from the MPE literature to assist shared decision-making where applicable, recognizing these tools were validated across mixed cancer cohorts [25]. Follow-up imaging and clinical review should be individualized according to tumor biology, prior treatments, and clinical course; there is no universally accepted CT surveillance interval for thoracic disease in ovarian cancer, reflecting heterogeneity of evidence [1].

Follow-up strategies should be individualized, as no consensus exists on optimal CT surveillance frequency for thoracic disease in ovarian cancer, reflecting heterogeneity in disease behavior and evidence gaps.

CONCLUSIONS

The peritoneal route remains the most widely recognized mechanism for the dissemination of ovarian cancer to the thoracic cavity. This pathway frequently results in clinical manifestations such as pleural effusion, pulmonary nodules, and other forms of thoracic metastases, all of which are indicative of advanced disease. Thoracic involvement has important implications for staging, clinical decision-making, and patient prognosis. Given these considerations, further high-quality clinical studies are needed to better characterize thoracic dissemination patterns and to improve early recognition of thoracic metastases. Enhanced understanding of these mechanisms will ultimately support more effective clinical management and more informed therapeutic planning.

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