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# Optimizing outcomes in symptomatic spinal metastases from non-small cell lung cancer: Evaluating the role of salvage surgical intervention in a multidisciplinary context - A Narrative Review

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## ABSTRACT

**Background:** Lung cancer, a leading cause of cancer-related mortality worldwide, often metastasises to the spine, resulting in significant morbidity and complex treatment challenges. The management of spinal metastatic disease from lung cancer necessitates a multidisciplinary approach, given the array of potential interventions including surgery, radiation therapy, chemotherapy, and supportive care. The selection of appropriate therapeutic strategies is influenced by multiple factors, including disease staging, patient health status, and symptomatology.

*Aim:* This review article aims to explore the current landscape of surgical intervention for spinal metastases from lung cancer, evaluating its role, efficacy, and the criteria for patient selection within the context of multidisciplinary care. Additionally, it seeks to provide an overview of the existing treatment modalities, highlighting the importance of a tailored approach based on individual patient needs.

**Methods:** An extensive review of the literature was conducted, focusing on studies, clinical trials, and meta-analyses published on the treatment of spinal metastases in lung cancer patients. Special attention was given to works discussing the surgical outcomes, prognostic factors, and the evolution of treatment protocols over recent decades.

**Results:** Surgical treatment for spinal metastases from lung cancer is beneficial for select patients, particularly

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those without prior systemic treatments and those in good overall health. The decision to pursue surgery should be made within a multidisciplinary team, taking into account the patient's specific situation and potential to benefit from the intervention. Research advancements and technological innovations continue to refine surgical techniques and improve patient outcomes.

*Conclusion:* While the role of surgery in treating spinal metastatic disease from lung cancer is limited, it remains a critical option for appropriately selected patients. Future research should aim to further define and expand the criteria for surgical candidacy, enhancing the precision of patient selection and tailoring of treatment strategies. Emphasis on a multidisciplinary approach is essential for optimising outcomes and advancing care for patients with this challenging condition.

**KEY WORDS:** *Non-small cell lung cancer; small cell lung cancer; spinal metastases; bone metastasis; spinal cord compression; osteolytic metastasis; surgical intervention; multidisciplinary approach*

## INTRODUCTION

Lung cancer stands as a predominant cause of mortality attributed to cancer worldwide, with classification into two primary types: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). A prevalent complication observed in the advanced stages of lung cancer is spinal metastasis, which involves the dissemination of cancer cells from the primary tumour site to the vertebral column. This condition results in significant clinical manifestations, including pain, neurological impairment, and a spectrum of other debilitating symptoms. Lung cancer is identified as the principal origin for approximately 80% of spinal metastases, positioning the skeletal system as the third most common site for cancer metastases, following the liver and lungs. Metastases of the osteolytic type, notably from the lung, kidney, thyroid, and gastrointestinal tract, are particularly concerning [1,2].

Extensive review of relevant literature and clinical observations have established that spinal metastases constitute the most frequent complication among cancer patients, affecting roughly 70% of individuals diagnosed with cancer. Given that lung cancer is the foremost cancer type to metastasise to skeletal structures, it is anticipated that a minimum of 40% of individuals with lung cancer will develop bone metastases throughout their disease trajectory [3]. The emergence of bone metastasis significantly impacts patients' independence, functionality, and quality of life, while also escalating disability, mortality rates, hospitalization costs, and duration of hospital stays [4,5]. Metastatic involvement of the vertebral column is recognised as a distressing condition that adversely affects morbidity, functional disability, and survival expectancy. Reports indicate that nearly half of the individuals succumbing to cancer have vertebral column metastases, with 10% experiencing spinal cord compression [6].

This manuscript aims to explore the clinical scenario of lung cancer metastasizing to the spine and the role of surgical intervention as a palliative measure in select cases. It is critical to underline that the option of surgical treatment remains a subject of debate, and the surgical approach is sometimes viewed with skepticism. This stems from the fact that surgical intervention is not traditionally included within the conservative management spectrum for lung cancer but is considered for cases exhibiting progressive neurological deficits [7].

## METHODOLOGY

In conducting this review, a comprehensive literature search was performed across several major databases, including PubMed, Scopus, and Web of Science, to gather relevant information on the surgical management of spinal metastases from non-small cell lung cancer. The search strategy employed a combination of keywords such as "non-small cell lung cancer," "spinal metastasis," "surgical treatment," "multidisciplinary approach," and "patient outcomes." The selection criteria were focused on articles published in English, with a particular emphasis on clinical trials, observational studies, and meta-analyses that discussed outcomes, prognostic factors, and the evolution of surgical and multidisciplinary treatments for spinal metastases in lung cancer patients. This methodological approach enabled the identification and synthesis of critical insights into the current state and future directions of surgical care for spinal metastases from non-small cell lung cancer.

## EPIDEMIOLOGY, PATHOPHYSIOLOGY AND DIAGNOSIS

Spinal metastasis represents a common complication in lung cancer, affecting approximately 20-40% of patients

in the advanced stages of the disease. The likelihood of developing spinal metastases escalates as lung cancer progresses, with a higher prevalence observed in individuals diagnosed with NSCLC compared to those with SCLC [3-5]. Approximately 60-70% of SCLC patients will have extensive disease at diagnosis, with a significant portion developing spinal metastases. SCLC's rapid growth and early dissemination patterns contribute to this higher rate of spinal involvement. However, while NSCLC has a lower overall metastatic rate at diagnosis compared to SCLC, the higher prevalence of NSCLC means it also contributes significantly to the number of spinal metastases cases [1-4]. The underlying mechanisms of spinal metastasis in lung cancer are intricate and involve multiple factors. Cancer cells can colonise the spine via hematogenous spread, lymphatic dissemination, or direct invasion of adjacent tissues. This metastatic involvement can lead to spinal cord or nerve root compression, manifesting as pain, neurological deficits, and a range of other clinical symptoms. Furthermore, pathological fractures of the spine due to metastatic lesions significantly contribute to patient morbidity [4,5].

Diagnosing spinal metastases in lung cancer poses considerable challenges and necessitates an integrated approach that includes detailed patient history, physical examination, and diagnostic imaging. Tools such as X-rays, computed tomography (CT) scans, and magnetic resonance imaging (MRI) are pivotal in the assessment and identification of spinal metastases. In certain scenarios, biopsy or the acquisition of tissue samples may be imperative to establish a definitive diagnosis [4-6].

## SURGICAL MANAGEMENT OF LUNG CANCER WITH SPINAL INVASION

Lung cancer frequently exhibits growth and intrathoracic spread, alongside metastases to various organs. Predominant metastatic sites include supraclavicular and inferior cervical lymph nodes, liver, brain, bones, and adrenal glands [4,5]. Approximately 40% of patients with lung cancer develop bone metastases, predominantly of the osteolytic type, leading to significant morbidity. This includes pathological fractures, nerve root compression, bone pain, spinal cord compression, neoplastic bone marrow infiltration, and hypercalcemia of malignancy. These complications arise from increased bone metabolism, primarily due to enhanced bone resorption, and are managed through radiation therapy, specific radioisotope administration, surgical intervention, and analgesic treatment [3].

The onset of lung cancer metastases to the vertebral column can occur at any stage of the disease, through direct extension, hematogenous spread, or lymphatic routes. While these tumours are generally considered incurable, advancements in technology have enabled the possibility of radical surgical interventions [2]. Remarkably, 10% of patients with vertebral metastases are unaware of their cancer diagnosis, with spinal cord compression often being the initial presenting symptom; 5% of these cases are due to lung cancer [7]. Lung tumours typically develop osteolytic metastases, demonstrating a tendency for osteotropy. The radiographic appearance of bone metastases varies based on the degree of osteolysis or bone formation, the primary tumour, and its location [9].

The impact of malignancies on the vertebral column includes structural weakness, ataxia, and severe pain, necessitating immediate surgical intervention for stabilization [10]. Primary lung tumours invading the spine can cause excruciating pain and Horner syndrome, with the pain intensifying as the cancer progressively destroys vertebral bodies [2,11].

Following the findings from a randomised trial by Patchell et al. in 2005, the importance of decompressive surgical resection in managing metastatic spinal cord compression has been established [12]. The goal of surgical treatment is to decompress the spinal canal by removing the tumour mass. This is complemented by minimally invasive techniques such as spondylodesis for vertebral column stabilization and spondylosyndesis through various surgical approaches, alongside kyphoplasty and stereotactic radiotherapy. Surgical management of vertebral metastasis is primarily palliative, focusing on spinal canal decompression and stability restoration [13].

Percutaneous vertebral augmentation techniques, like percutaneous kyphoplasty (PKP) and percutaneous vertebroplasty (PVP), offer minimally invasive alternatives for managing painful spinal metastases, especially in high-risk patients [14,15]. Studies by Zhang et al. have shown PKP to significantly correct kyphosis compared to conservative treatments, providing substantial pain relief and functional improvement while preventing further local kyphotic deformation [15]. Direct decompressive surgery followed by postoperative radiotherapy has proven more effective than radiotherapy alone in improving muscle strength, functional capability, and overall survival rates [16].

However, the utility of PKP in a palliative setting does not extend to improving patient survival rates, despite enhancing quality-adjusted life years (QALY) and indicating improved life quality post-treatment [17]. The surgical approach for lung tumours invading the spine and its contribution to cancer therapy remains a topic of debate, with clinical evidence indicating poor survival

rates post-surgical treatment for spinal involvement due to lung cancer [10,17].

It is crucial to evaluate prognostic factors in the decision-making process for treating bone metastases in lung cancer. Tokuhashi et al. proposed six prognostic factors for assessing survival chances in patients with metastatic vertebral column tumours, including (i) the number of vertebral metastases, (ii) the presence of internal organ translocations, (iii) the severity of spinal cord paralysis, (iv) the patient's overall health condition, and (v) the presence of non-vertebral bone metastases [18].

The revised Tokuhashi, Tomita, modified Bauer, and Oswestry scores are frequently utilised as tools for predicting the survival of patients with spinal metastases and assisting in the decision-making process concerning surgical interventions [19-22]. Nevertheless, these prognostic indicators often provide a prognosis for patients with lung cancer that is more pessimistic than warranted. Studies showed that the Tokuhashi scores outperformed the Tomita score; nonetheless, they continued to provide prognostic estimates that were too low for 35% to 40% of the patients [23].

Other prognostic factors, including the number of bone metastases, the primary tumour's malignancy degree, and visceral metastasis to major organs, play a critical role in assessing the feasibility and utility of surgical interventions in the vertebral column [20]. Prognosis remains particularly poor for patients with bone metastases, metastases to vital organs, and direct spinal invasion, especially in cases of superior sulcus tumours [24-27]. Therefore, the decision to proceed with surgical intervention in patients with lung cancer invading the spine requires a multidisciplinary approach. Considerations for total vertebrectomy should be discussed when direct invasion involves 30% or less of the vertebral cortical bone, with preoperative and postoperative chemoradiotherapy deemed sufficient for disease recurrence prevention [28].

In conclusion, the surgical management of lung cancer with spinal invasion is complex and controversial, potentially beneficial for severe pain management and tumour recurrence control [29,30]. Complete resection and multilevel laminectomy may be proposed for extensive tumour invasion, while partial vertebrectomy is suggested for less extensive tumour involvement. This underscores the need for aggressive, multidisciplinary surgical strategies, particularly for superior sulcus tumours with vertebral invasion, to improve prognosis and survival rates [31-33].

## DISCUSSION

Presently, lung cancer is acknowledged as one of the deadliest cancers, with spinal metastases deemed generally incurable. Metastatic spread to the thoracic spine from lung cancer, which can occur via lymphatic or hematogenous routes, is notably frequent [34]. The consideration of surgical intervention for metastatic lung cancer infiltrating the spine presents a formidable challenge, marked by debate. The characteristics of the metastasis, including the organs involved, extent of infiltration, number of bone metastases, severity of spinal cord impairment, and level of pain, are critical prognostic factors that influence both the surgical outcomes and the patient's survival prospects [34,35].

The prognosis plays a pivotal role in deciding the appropriateness of surgical intervention. Consequently, there's a notable hesitancy to opt for surgery in patients with a limited life expectancy, compounded by a scarcity of studies and data supporting surgical intervention in such patient demographics [35]. The prognostic scoring systems developed in the 1990s and early 2000s, such as the Tokuhashi score, are commonly utilised to assess patients with a grim prognosis. However, the reliability and predictive accuracy of these tools have been questioned, as they often fail to accurately forecast survival, leading to potential underutilization in surgical candidate selection [35,36]. Lee et al. highlighted that the actual survival of patients frequently surpassed the expectations set by the revised Tokuhashi score, suggesting an improvement in survival rates due to advancements in medical and surgical oncology, which complicates the prognosis prediction [37]. Therefore, it is crucial to reevaluate the exclusion criteria to ensure that patients who could benefit from surgery are not inadvertently overlooked.

In the surgical treatment planning process, spine surgeons should be mindful of the tendency to underestimate patient survival. Notably, patients who have not previously received systemic treatment might benefit more substantially from surgery. Factors such as low BMI, indicative of a cachectic state, may predict a worse prognosis and should be considered in the evaluation process. Ideal surgical candidates include those with adenocarcinoma amenable to targeted therapies, candidates for denosumab treatment, individuals in good general health, and those yet to undergo systemic treatments [23].

Historically, surgical treatment for lung cancer with spinal invasion has yielded disappointing long-term outcomes concerning both mortality and morbidity, particularly in advanced-stage patients. Such conditions have been characterised as incurable and unresectable, with a poor long-term prognosis, especially in cases of vertebral invasion by superior sulcus tumours [38]. However, Yokomise et al. reported that advancements in technology and the introduction of novel surgical techniques have

the potential to enhance surgical outcomes [32]. Recent studies have demonstrated the efficacy of multimodal treatment, including surgical resection for selected patients with superior sulcus tumours involving the spine, showcasing safe procedures with promising survival rates following concurrent chemoradiotherapy (CRT) and surgical resection, resulting in a 5-year overall survival (OS) and disease-free survival (DFS) rate of 55% and 40%, respectively [39].

Park et al. aimed to analyse survival and functional outcomes post-surgery in patients with spinal metastases and limited life expectancy, reviewing 492 surgical cases across different time frames. The study found a significant improvement in median survival, particularly in the latest period studied (2013–2020), with notable survival enhancements for lung and kidney cancer cases within this timeframe [40]. Moreover, hybrid therapy involving separation surgery followed by stereotactic body radiation therapy in NSCLC patients with metastatic epidural spinal cord compression has shown high local control rates and survival benefits when combined with Epidermal Growth Factor Receptor (EGFR) -targeted treatments initiated post-hybrid therapy [41].

A recent meta-analysis systematically reviewed prognostic factors and outcomes of surgical intervention for lung cancer patients with spinal metastases, covering 14 studies and 813 patients. The analysis identified preoperative ambulatory status and the number of involved vertebrae as significant prognostic factors influencing survival. The study suggests that patients with an adequate expected survival period could gain from surgical intervention, particularly when combined with adjuvant therapies [42].

Consequently, a deeper understanding of metastatic disease pathophysiology and technological advancements has the potential to refine surgical techniques, improving prognosis and extending survival for appropriately selected patient groups. Despite the constrained role of surgery in the overarching management of spinal metastatic disease from lung cancer, its potential benefits for specific patient cohorts should not be overlooked. Future perspectives should focus on refining patient selection criteria and enhancing surgical techniques through research and technological advancements. These efforts promise to better delineate the role of surgery within a multifaceted treatment approach, aiming for improved survival rates and quality of life for patients facing this challenging diagnosis.

## CONCLUSION

The surgical approach, while not the universal standard, plays a pivotal role in the management of spinal metastatic disease from lung cancer for select patients. This necessitates precise diagnosis and tailored interventions, considering the disease's stage, patient's health, and symptom severity. Treatment strategies, often encompassing surgery, radiation, chemotherapy, and supportive care, aim to alleviate symptoms and enhance life quality. Identifying candidates for surgery requires a multidisciplinary approach, emphasizing the need for collaborative planning and evaluation by a team of specialists to ensure the most beneficial outcomes. Ongoing research is crucial to unravel the complexities of spinal metastasis and to innovate more effective treatments. Understanding the mechanisms of metastasis and improving therapeutic options will ultimately enhance patient management and prognosis. Thus, while surgery offers significant benefits for certain patients, its application should be carefully considered within a comprehensive, patient-focused, and multidisciplinary treatment framework.

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