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Review

Emerging and established clinical, histopathological and molecular parametric prognostic factors for metastatic spine disease secondary to lung cancer: Helping surgeons make decisions

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ABSTRACT

Metastatic lung cancer to the spine occurs at high rates with patients usually given poor prognoses. Recent studies have observed that patients with certain genetic and molecular aberrations have better responses to adjuvant therapy. As such, current metastatic spine disease treatment algorithms grading all lung primaries' prognosis as poor may lead to inadequate treatment of spinal metastases. The aims of this study are to determine current survival patterns in metastatic spine disease secondary to lung cancer and identify relevant parameters that influence the prognostication of these patients. A systematic review in accordance with PRISMA guidelines was conducted for literature published between January 1, 1996 and September 31, 2015. The 27 studies identified were Level IV retrospective studies with an overall 'low' level of evidence. The overall median survival of patients with spine involved metastatic lung cancer was poor, ranging from 3.6 to 9 months. Median survival of patients with non-small cell lung cancer being treated with epidermal growth factor receptor (EGFR) inhibitors were observed to be better, with survival of up to 18 months. This review reports a subset of lung cancer patients with oncogenic molecular mutations that appear to confer a better overall survival. In these patients, individualized assessment rather than strict adherence to current metastatic scoring algorithms when determining management may be preferred.

1 Introduction

Lung cancer is the leading cause of cancer-related death in the world [1,2]. Metastatic bone tumours, especially to the spine, occur at high rates in lung cancer and are often in advanced stages of the disease when presenting with spinal metastases. The surgical treatment of metastatic lung cancer to the spine is frequently palliative and focussed on the restoration or preservation of neurological function, ensuring mechanical stability, and providing pain relief [3].

Historically, most studies report poor survival rates in patients with metastatic lung cancer to the spine, making surgery at times difficult to contemplate. Traditionally, life expectancy greater than 3 months with reasonable quality of life are prerequisites for surgery is to be considered [4]. Multiple classification and treatment algorithms have been developed around patient prognosis to assist the surgeon in determining whether surgery is indicated. They are

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Table 1
Inclusion and exclusion criteria for studies describing the clinical, histopathological and molecular parametric prognostic factors for metastatic lung cancer affecting the spine

Study component	Inclusion	Exclusion
Participants	Age ⩾ 18 years	Age < 18 years
	A pathology of spine column or spinal cord metastases secondary to lung cancer	A pathology of inflammation, infection or trauma
Interventions and comparators	Patients undergoing surgery or radiation therapy or chemotherapy treatment or no treatment for their spine column or spinal cord metastases	For not analyzing the metastatic spine disease from lung cancer separately
	Classification systems or treatment algorithms guiding management of spine metastases secondary to lung cancer	
Outcomes	Life expectancy and multivariate prognostic factors specific to patients with spine column and or spinal cord metastases secondary to lung cancer	For not including the outcome of interest
Study designs	RCT, clinical case series, reviews	Case reports
Publication	Study published in English, in a peer-reviewed, PubMed-indexed journal	Abstracts, editorials, letters and duplicate study or repeat publication of same patient group

based on one or more of the following: (1) general well-being or the burden of disease, (2) spread of disease, (3) spinal stability and (4) neurological state of the patient. Recently with the emergence of tumour molecular sequencing and genetic profiling, oncologists are able to utilize targetted therapies to improve the life expectancy of specific tumours. This rapidly evolving science challenges the validity of many of the previously developed classifications designed to predict prognosis in patients with metastatic spine disease.

Previously, patients diagnosed with lung cancer were classified either as small cell (SCLC) or non-small cell lung carcinoma (NSCLC). NSCLC were further classified as squamous cell carcinoma, adenocarcinoma, large cell, or not otherwise specified (NOS). The lumping of all NSCLC together despite different histological patterns was largely due to the fact that therapies were not specific for different histologies with survival thought to be similar. More recently genomics has afforded higher specificity when compared to the traditional dichotomy of small cell and non-small-cell lung cancer. By identifying genetic aberrations, a greater number of lung cancer subsets can be identified; of which individual lifespan can be extended if favourable respond to targetted therapy is attained.

It is critical that spine surgeons are up to date and aware of prognostic factors portending greater survival in patients with metastatic lung cancer so they can provide appropriate information and interventions to improve health-related quality of life. Constantly improving oncological treatment and the innovation of new surgical techniques including minimally invasive surgery (MIS) provides the potential for new paradigms in the treatment of lung cancer patients with metastatic spine disease. Current metastatic spine algorithms grading all lung primaries, as poor prognosis is potentially inaccurate because of newly identified lung cancer subsets and targetted therapy. This systematic review aims to translate all current evidence to determine the current survival patterns in patients with metastatic spine disease secondary to lung cancer and to identify relevant clinical, histopathological and molecular parameters that influence the prognostication of these patients.

2. Methods

2.1. Electronic database search strategy

A systematic computer-based search was performed of the following databases: PubMed, EMBASE, the Cochrane Library, and Google Scholar. All entries from January 1, 1996 to September 31, 2015 were searched. The search was limited to literature published in the English language. Table 1 describes the inclusion and exclusion criteria of this study. The focus of this study was to systematically review all published literature discussing the clinical, histopathological and molecular parameters correlating to the life expectancy and prognosis of patients suffering from spinal metastatic disease secondary to lung cancer. We used the following Medical Subject Headings (MeSH) terms (all in the "explode" function): "spine metastases" or "spinal column metastases" or "spinal cord metastases" AND "lung neoplasm" or "lung cancer" or "lung carcinoma" AND "survival" AND "prognosis" or "life-expectancy" or "epidermal growth factor receptor (EGFR)" or "genetic markers" or "molecular".

2.2. Inclusion and exclusion criteria

Three clinicians (CF, JT and NB) independently reviewed the abstracts and selected them for detailed assessment of the full articles. Abstracts were selected if they fulfilled the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [5] and reported on the pathology of spine column or spinal cord metastases secondary to lung cancer in relation to management options, treatment and outcome. Study designs included were randomized controlled trials (RCT), clinical case series and review articles. The abstracts had to be written in the English language and published in a peer-reviewed, Pubmed-indexed journal. Any differences in opinion by the reviewers were resolved by discussion.

2.3. Data extraction

Data extracted included: (1) study design and general demographics, (2) clinical, histological and histological parameters, (4) independent prognostic factors, (5) cohort survival descriptions, (6) treatment outcomes.

2.4. Study quality and overall strength of body of literature

Levels of Evidence (LoE) ratings were assigned to each article by the reviewers accounting for methodological quality and sources of bias based on recommendations made by the Agency of Healthcare Research and Quality (AHRQ) [6–9]. The overall body of evidence was based on the recommendations of the AHRQ and Grades of Recommendation Assessment, Development and Evaluation (GRADE) Working Group [10–12]. The final overall strength of the literature is a measure of our confidence that the effect size closely matches the true effect and is stable [13]. The quality of the literature was graded high, moderate, low, or insufficient as outlined elsewhere [12]. Briefly, the overall body of evidence was considered 'high' when the majority of studies was Class I or II and indicates that the confidence level was very high and that the true effect lies close to the estimated effect. The overall body of evidence was considered 'low' if the majority of studies was Class III or IV and indicates that the true effect may be substantially different from the estimated effect. A rating of 'insufficient' was