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Comprehensive Analysis of Bone Metastases in Lung Cancer: A Systematic Review Protocol

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ADMINISTRATIVE INFORMATION

Support - No support or grants were received.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202490108

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 September 2024 and was last updated on 24 September 2024.

INTRODUCTION

Review question / Objective What are the most frequent demographic and clinical characteristics in lung patients who develop bone metastasis and how they affect prognosis and survival of these patients?

Rationale Lung cancer is the leading cause of cancer-related deaths, and metastatic carcinoma is the most frequent malignant bone tumor. Furthermore, bone is one of the most frequent sites of metastasis in patients with lung carcinoma. The occurrence of skeletal-related events is prevalent among these patients and results in high morbidity and a reduced quality of life. In this context, bone metastasis is currently a topic of increasing debate in lung cancer. The characterization of bone metastasis, the estimate survival and prognostic factors are important to predict skeletal related events risk and survival and help to decide whether orthopedic surgery is indicated for these patients. Most studies on bone

metastasis are conducted with patients with metastatic carcinoma from different primary sites in the same sample. There is a lack of studies addressing this specific topic of bone metastasis from lung cancer. Furthermore, there is no published systematic review regarding the characterization of bone metastasis from lung carcinoma. Thus, we designed this protocol to characterize bone metastases, estimate skeletal events, survival and prognostic factors of these patients. This information may be useful for better understanding of the disease course, guiding early surveillance for detection or interventions in high-risk groups that can improve patients' quality of life and survival.

Condition being studied Bone metastasis from lung carcinoma.

METHODS

Search strategy The search strategy will be conducted using MEDLINE/PubMed, covering the

period from the database's inception to the end of September 2024. There were no language restrictions applied in searches.

The search terms include a combination of MeSH terms and keywords related to "lung cancer", "bone metastasis", and "prevalence", and their synonyms. Filters will not be applied to exclude any specific types of studies. The search results will be then screened for relevance based on titles and abstracts, with full-text reviews conducted where necessary. The full search strategy is present in Appendix 1, ensuring comprehensive coverage of relevant studies.

Participant or population Studies involving patients with lung carcinoma will be included in this review.

Intervention No intervention is associated with this evidence synthesis.

Comparator When comparisons are necessary, groups will be stratified by the presence of bone metastasis to identify relevant characteristics.

Study designs to be included Cohort, case-control and cross-sectional studies.

Eligibility criteria Cohort, case-control, and cross-sectional studies involving lung cancer patients focusing on incidence, risk factors and survival. The study must provide epidemiological, clinical and histological characteristics in the groups of patients with and without bone metastases to be eligible for data extraction in this protocol. This criterion will be applied to obtain data measures of broad characterization of bone metastases from lung cancer.

We will employ an independent, duplicate process for study selection. Since the systematic review will be initially conducted exclusively using PubMed, no duplicate records are expected to be identified. In cases of divergence, differences will be resolved through discussion and consensus.

Information sources MEDLINE/PubMed.

Main outcome(s) The variables of interest in this study are gender, age, smoking, comorbidities, plasma hemoglobin concentration, performance status, histology, staging, other primary tumor, location and number of bone metastases, time from diagnosis of the primary tumor to bone metastasis, other sites metastases, skeletal related events (bone pain, pathological fracture, hypercalcemia, need for radiotherapy or surgery) and death.

Data management For data management, each reviewer will independently handle studies using a Google Sheet that is distributed and supervised by an external data manager. If necessary, Rayyan will be utilized to expedite the eligibility assessment phase.

Quality assessment / Risk of bias analysis We will assess the risk of bias in the included studies using the Newcastle-Ottawa Scale (NOS). The NOS is specifically designed for evaluating non-randomized studies, such as cohort and case-control studies, which are expected to be more common in the literature we will be reviewing.

The NOS assessment will be structured around three domains:

Selection of study groups: we will evaluate how the studies selected their cohorts, focusing on the representativeness of the exposed cohort, the selection of the non-exposed cohort, and the ascertainment of exposure.

Comparability of groups: we will assess the comparability of the cohorts based on the design and analysis, mainly considering how the studies controlled for confounding factors.

Ascertainment of outcomes: we will examine how outcomes were determined, including the methods used for outcome assessment, the completeness of follow-up.

Each study will receive a score based on these criteria, allowing us to determine the overall risk of bias for the individual studies.

Strategy of data synthesis In this systematic review, we will conduct a comprehensive synthesis of the available evidence on factors related to bone metastasis in lung cancer, focusing on descriptive analysis rather than quantitative meta-analysis. Through our primary aim established to summarize key factors associated with metastasis, we plan to inform future research and potential meta-analyses. The data synthesis will involve a narrative approach, systematically describing the study characteristics, methodologies, and findings of the included studies. We plan to identify patterns, trends, and gaps in the literature, with particular attention to variations in study design, population characteristics, and outcome measures. Given the nature of this review, meta-bias assessments and confidence evaluations (e.g., GRADE system) will not be carried in our methodology.

Subgroup analysis The primary subgroup stratification for descriptive and exploratory analyses will be based on the presence or absence of bone metastasis. The main stratification for

descriptive and exploratory analyses will be based on the presence of bone metastasis.

Sensitivity analysis No sensitivity analysis is planned for this systematic review.

Language restriction There will be no language restrictions during the search and retrieval of studies. However, only publications in English, Portuguese or Spanish will be selected for data extraction.

Country(ies) involved Brazil.

Other relevant information Lung neoplasm; Neoplasm metastasis Systematic review.

Keywords Lung neoplasm; Neoplasm metastasis Systematic review.

Contributions of each author

Author 1 - Francesca Ramundo - Conceptualization, study design, coordination of data collection, and analysis, data interpretation.

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Author 2 - Pedro e Silva - Data collection, data management, and database maintenance.

Author 3 - César Fontenelle - Manuscript drafting and integration of co-author feedback.

Author 4 - Daniel Umpierre - Statistical analysis, data interpretation, and data visualization.

Author 5 - Marcelo Oliveira - Conceptualization, study design, and research coordination, data collection.

Author 6 - Fernanda Mello - Conceptualization, study design, manuscript review.