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Association of Lung Cancer Histology with Developing Bone Metastasis: A Systematic Review Protocol

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ADMINISTRATIVE INFORMATION

Support - No dedicated support is planned.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202490007

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 2 September 2024 and was last updated on 2 September 2024.

INTRODUCTION

Review question / Objective What are the most prevalent demographic, clinical characteristics, and cancer histology in lung cancer patients who develop bone metastasis?

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, which results in a high morbidity and a reduced quality of life. In this context, bone metastasis is currently a topic of increasing debate in lung cancer. However, there are few studies regarding the influence of lung cancer histology on the frequency and characteristics of bone metastasis. Approximately 40% of patients with lung carcinoma develop bone metastasis, and adenocarcinoma is the most frequent histological subtype. Although a few studies have specifically compared the risk of bone metastasis according to the histological subtypes among patients with lung cancer, several studies have assessed the frequency of bone metastases and the histological subtypes of lung cancer using various approaches. Nevertheless, to our best knowledge, there is no published systematic review regarding an association between histology and skeletal complications in this malignancy. Thus, we designed this protocol to assess whether lung cancer histology influences the occurrence of bone metastasis from lung cancer. This information may be useful for guiding early surveillance for detection or interventions in high-risk groups that can improve patients' quality of life and survival.

Condition being studied Lung cancer, regardless of histological type.

METHODS

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

period from the database's inception to the end of August, 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 cancer, regardless of histological type, will be included in this review.

Intervention No intervention is associated with this evidence synthesis.

Comparator When comparisons are needed, groups will be stratified by the presence of bone metastasis or cancer histological type 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 lung cancer histological subtype frequency in the groups of patients with and without bone metastasis to be eligible for data extraction in this protocol. This criterion will be applied in order to obtain data measures of association between lung cancer histology and the frequency of bone metastases.
We will employ an independent, duplicate process for study selection. Since the systematic review will be initially conducted exclusively using MEDLINE/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 demographic and clinical characteristics of the lung cancer patients gender, smoking, histology, staging and bone metastases occurrence.

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.

Keywords Lung neoplasm; Neoplasm metastasis; Systematic review.

Contributions of each author

Author 1 - Marcelo B. d. R. Oliveira - Conceptualization, study design, and research coordination.
Author 2 - Francesca B. Ramundo - Conceptualization, study design, coordination of data collection, and analysis, data interpretation.
Author 3 - Pedro D. C. S. Silva - Data collection, data management, and database maintenance.
Author 4 - Bruno S. Queiroz - Data collection, data management, and database maintenance.
Author 5 - Ana C. C. C. Caetano - Data collection, data management, and database maintenance.
Author 6 - César R. d. C. Fontenelle - Manuscript drafting and integration of co-author feedback.
Author 7 - Daniel Umpierre - Statistical analysis, data interpretation, and data visualization.
Author 8 - Fernanda C. d. Q. Mello - Conceptualization, study design, manuscript review.