Lung Cancer 96 (2016) 19–24

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

The relationship between lung cancer histology and the clinicopathological characteristics of bone metastases

Marcelo Bragança dos Reis Oliveira[a,*], Fernanda Carvalho de Queiroz Mello[b,c], Marcos Eduardo Machado Paschoal[c]

[a] Trauma-Orthopaedics Service, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
[b] Faculty of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
[c] Thoracic Diseases Institute, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil

ARTICLE INFO

Article history:
Received 1 December 2015
Received in revised form 3 February 2016
Accepted 25 March 2016

Keywords:
Lung cancer
Bone metastasis
SRE
Histology

ABSTRACT

Objectives: Lung cancer is the leading cause of death due to cancer, and bone is one of the most frequent sites of metastasis. However, there is no published evidence regarding an association between lung cancer histology and skeletal complications. Therefore, we evaluated the influence of lung cancer histology on the frequency of bone metastases (BMs), skeletal-related events (SREs), and survival after BM.
Material and methods: This retrospective study evaluated medical records from 413 patients who were diagnosed with lung cancer between 2003 and 2012. The prevalences of BMs and SREs were calculated, and their associations with the histological subtypes were evaluated using the chi-square test, odds ratios (OR), and 95% confidence intervals (CI). Overall survivals and associations with the histological subtypes were evaluated using the Kaplan-Meier method and the log-rank test.
Results: The prevalences of BM, synchronous BM, and SREs were 28.2%, 70.4%, and 68.7%, respectively. Adenocarcinoma was the most common histological subtype (46.7%), and was significantly more frequent among patients with BM (58.3% vs. 42.1%; p = 0.003; OR: 1.92; 95% CI: 1.29–2.97). Squamous cell was significantly less frequent among patients with BM (13.0% vs. 29.8%; p = 0.0004; OR: 0.35; 95% CI: 0.19–0.64). The median survival time after the first BM diagnosis was 4 months, and there was no significant difference in the survival periods for the various histological subtypes.
Conclusion: Adenocarcinoma and squamous cell were significantly associated with higher and lower risks of developing BM, respectively.

1. Introduction

Lung cancer is the leading cause of cancer-related deaths, and metastatic carcinoma is the most frequent malignant bone tumor, which occurs in approximately 15–40% of patients with lung cancer [1,2]. Furthermore, bone is one of the most frequent sites of metastasis, which results in a high morbidity and a reduced quality of life among these patients [3–5]. In this context, osteoclast inhibition using bone target agents (BTAs), such as bisphosphonates and denosumab, is currently a topic of increasing debate in lung cancer [4–6]. However, there are few studies regarding the influence of lung cancer histology on the frequency and characteristics of bone metastasis (BM). Recent studies have demonstrated that BTAs are associated with a reduction in the risk of, and time to, skeletal related events (SREs) among patient with non-small cell lung cancer (NSCLC) [7–11] and possibly with an increased survival [12]. However, their routine use in patients with BM from lung cancer remains relatively low [5,6].

Approximately 40% of patients with NSCLC develop BM, and adenocarcinoma is the most frequent histological subtype [2,13–17]. Although no studies have specifically compared the prevalence of BM according to the histological subtypes among patients with NSCLC or small cell lung cancers (SCLC), several studies have assessed the frequency of BM and the histological subtypes of lung cancer using various approaches. Nevertheless, to our best knowledge, there is no published evidence regarding an association

Abbreviations: BTA, bone target agent; BM, bone metastasis; SRE, skeletal-related event; NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; LC, large cell carcinoma; NOS, not otherwise specified; Adeno, adenocarcinoma.

* Corresponding authors at: Serviço de Traumato-Ortopedia do Hospital Universitário Clementino Fraga Filho da Universidade Federal do Rio de Janeiro. Rua Rodolpho Paulo Rocco, 255, Cidade Universitária – Ilha do Fundão, Rio de Janeiro. RJ, CEP: 21941-913 Brasil.
E-mail addresses: marreis@bol.com.br, marceloreis@hucff.ufrj.br (M.B.d.R. Oliveira).

http://dx.doi.org/10.1016/j.lungcan.2016.03.014
0169-5002/

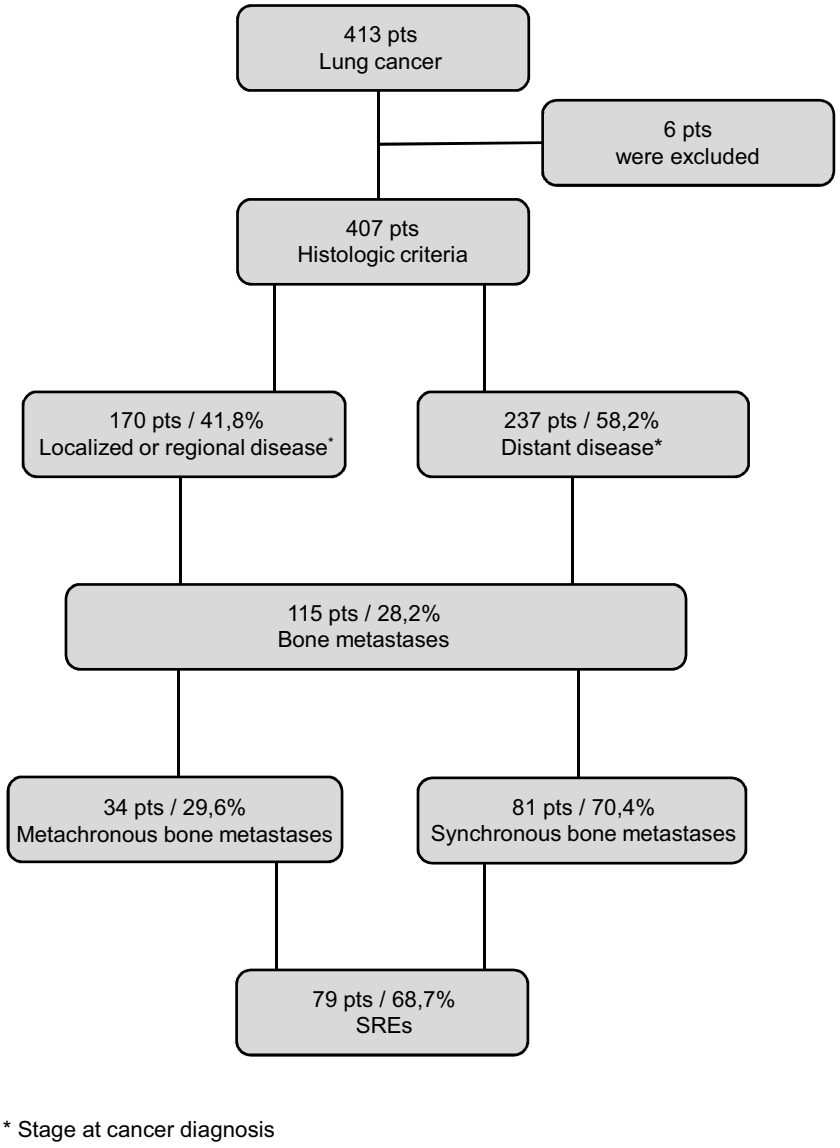

Fig. 1. Cohort diagram—Lung cancer patients according to the stage at cancer diagnosis, the presence of bone metastases at diagnosis or throughout follow-up, and skeletal-related events (SREs).

between histology and skeletal complications. Thus, we designed this study to assess whether lung cancer histology influenced the occurrence of BM and SREs, as well as the overall survival of patients with BM, in a cohort of patients who had not been routinely treated using BTAs. This information may be useful for guiding early surveillance for BM detection or interventions in high-risk groups that can improve patients' quality of life and survival.

2. Material and methods

2.1. Study population

This retrospective study's design was approved by our institutional ethics review board. We retrospectively evaluated medical records from 413 patients who were diagnosed with malignant primary lung tumors at our institution between January 2003 and January 2012. The inclusion criteria were pathological confirmation of NSCLC or SCLC and complete tumor staging data. To accurately evaluate the association with survival, we excluded patients who were diagnosed with a second malignant primary tumor or had an unknown date of death. Lung carcinoma was classified according to histological subtype, using the World Health Organization classifications: adenocarcinoma, squamous cell, large cell (LC), NSCLC not otherwise specified (NOS), and SCLC [18].

The events of interest were the occurrence of BM, SREs, and death. BMs were diagnosed via histopathologic examination of bone biopsy samples or via Tc^{99-}bone scintigraphy with two additional imaging modalities (X-ray radiography, computed tomography, or magnetic resonance imaging). SREs were defined as the need for radiotherapy, pathological fracture, spinal cord compression, the need for surgery due to BM, or hypercalcemia. BMs were classified as synchronous or metachronous according to the times of diagnosis for the first BM and the lung cancer. The minimum follow-up period after a diagnosis of BM was 24 months (excluding cases of death before 24 months).

2.2. Statistical analysis

The chi-square test was used to compare the proportions of histological subtypes among patients who did and did not develop BM, synchronous BM, SREs, or pathological fracture. The relationship between histological subtype and the occurrence of BMs was