

Research Article

Association between Osteoporosis and Bone Metastasis among Newly Diagnosed Lung Cancer Patients Based On Opportunistic Screening in Low-Dose Computer Tomography: The Results of the Retrospective Cohort Study

Yongli Li*

Xi'an Hospital of Traditional Chinese Medicine, China

*Corresponding author

Yongli Li, Xi'an Hospital of Traditional Chinese Medicine, China

Submitted: 23 March 2026

Accepted: 02 June 2026

Published: 03 June 2026

ISSN: 2578-3351

Copyright

© 2026 Li Y

OPEN ACCESS

Keywords

- Osteoporosis
- Bone metastasis
- Lung cancer
- Low-dose CT
- QCT

Abstract

This retrospective study explored osteoporosis-bone metastasis association in newly diagnosed lung cancer. 400 subjects underwent LDCT+QCT for osteoporosis diagnosis; survival and Cox analyses were used. Precancer osteoporosis (HR=3.30, $P<0.01$) increased bone metastasis risk and shortened its onset time, while surgery (HR=0.31, $P<0.01$) was protective. Early osteoporosis screening in these patients is recommended.

Aim: Opportunistic osteoporosis screening in China is more cost-effective when using low-dose chest CT (LDCT) combined with quantitative computed tomography technology (QCT). We retrospectively investigated the association between osteoporosis and bone metastasis in patients with newly diagnosed lung cancer.

Materials: Four hundred healthy individuals underwent LDCT screening, which was ultimately confirmed through histological and cytological diagnosis. QCT post-processing software was used to examine the trabecular bone volume density (vBMD), and osteoporosis was diagnosed according to the diagnostic criteria for osteoporosis by the American Society of Radiology using QCT imaging. Kaplan-Meier survival analysis was used to assess survival time, and Cox proportional hazards regression analysis was employed to ascertain the factors linked with bone metastases.

Results: COX univariate and multivariate regression analyses revealed that newly diagnosed lung cancer patients with osteoporosis (HR, 3.30; 95% CI, 1.90- 5.73; $P<0.01$) and surgery (HR, 0.31; 95% CI, 0.17- 0.57; $P<0.01$) were associated with a difference in the risk of bone metastasis. Compared to individuals without precancerous osteoporosis and surgery, the median time for the development of bone metastasis was shorter for those with precancer osteoporosis and those without surgery (median time to bone metastasis development, 35 months; 95% CI, 26-NA months; 44 months; 95% CI, 31-NA months; $P<0.01$).

Conclusions: Newly diagnosed lung cancer with osteoporosis is associated with a risk of bone metastasis and accelerated progression of bone metastasis. Our findings highlight the need for early identification of osteoporosis among newly diagnosed lung cancer patients.

INTRODUCTION

Bone metastasis is the leading cause of mortality in patients with lung cancer. Approximately 30% of lung cancer patients develop bone metastasis during treatment [1]. Approximately 50% of these patients inevitably develop bone pain, pathological fractures, bone marrow damage, and other skeletal events within one month of the onset of bone metastases. This significantly impacts the quality of life and increases the risk of death [2]. Consequently, identifying risk factors and understanding

the pathogenesis of bone metastasis in lung cancer, early detection of high-risk patients, aggressive management of bone metastasis, and decreasing the mortality rate among lung cancer patients are clinically significant.

Currently, the “seed-soil” hypothesis remains applicable in elucidating the mechanism underlying the migration of tumor cells from the primary site to the target organ [3]. The seeds could be tumors or specific cancer stem cells [4]. Simultaneously, soil refers to substances that supply energy for the metastasis of tumor cells, such

as bone marrow adipocytes and adipocytokines. Fernandez et al. [5], indicated that the original tumor cells modified the plasticity of bone marrow mesenchymal cells, creating a pre-metastatic niche for the invasion and proliferation of lung cancer bone metastasis in the bone. The accumulation of bone marrow adipocytes increases with age, intensifying age-related inflammation and deteriorating bone health due to alterations in the bone marrow microenvironment, leading to bone density loss [6]. It remains unclear whether the plasticity of bone marrow mesenchymal cells induces secondary changes in the bone microenvironment or whether age-related osteoporosis and changes in the bone microenvironment offer a fertile "soil" for tumor cell metastasis.

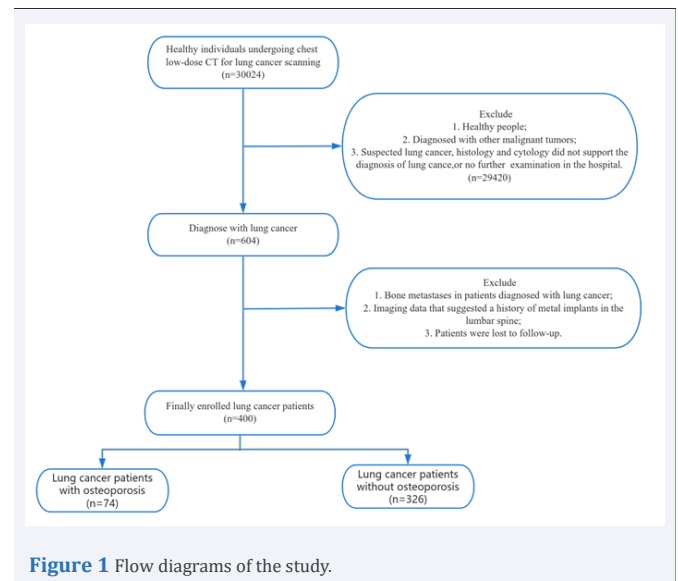
Assessment techniques for osteoporosis mainly include dual-energy X-ray absorptiometry, MRI bone microstructure imaging, and QCT [7]. Researchers are increasingly utilizing low-dose CT in conjunction with QCT to assess bone mineral density as part of opportunistic osteoporosis screenings. Compared with traditional osteoporosis technology, LDCT opportunistic screening for osteoporosis is twice as effective as dual-energy X-ray absorptiometry. It can detect early osteoporosis in men [8].

In this study, we utilized LDCT data for opportunistic osteoporosis to investigate the association between osteoporosis and progression to bone metastasis in patients with newly diagnosed lung cancer.

METHODS

Study design

The data was from a large-scale data study carried out through QCT and LDCT of the chest in the check-up population. Chest LDCT is primarily utilized for lung cancer screening. The vBMD is acquired by integrating the data of chest LDCT with QCT technology. The patients with suspected lung cancer, as indicated by the LDCT data and ultimately diagnosed with lung cancer through pathological and histological examinations at the hospital were included. The vBMD of lung cancer patients was measured by QCT technology. Eventually, 400 lung cancer patients were included in this study, among whom 74 patients had osteoporosis concurrently at the time of lung cancer diagnosis Figure 1. We received approval from the local ethics committee (Ethical Approval Number: 2021 Aaron trial Examination No. (68)). The study was conducted per the Declaration of Helsinki. The exclusion criteria were the following: (1) bone metastases in newly diagnosed lung cancer patients; (2) imaging data indicating a previous presence of metal implants in the lumbar spine; (3) patients were lost to follow-up.



LDCT scanning

All LDCT scans were conducted using a 64-slice CT machine (Lightspeed, General Electric, US) for helical scanning, which was independently performed by radiology scanning technicians. The scanning parameters of the vertebral body were tube volt-age 120KV, tube current 100mA, slice thickness 1 mm, scanning field of view 500 mm× 500 mm, and matrix 512 × 512. Image reconstruction was performed using standard reconstruction algorithms. The scanning data were saved in the Picture Archiving and Communication System (PACAS) system of the radiology department in Digi-tal Imaging and Communications in Medicine (DICOM). Data and the image were transmitted to the QCT image workstation at the same time.

Measurement of bone density

All vBMD measurements were performed in QCT Pro (Mindways Software, inc, Austin, TX, USA) by trained professionals in QCT image analysis or by radiologists with more than three years of experience. Image analysis and scanning were performed on the same day, and LDCT scan data were imported in DICOM format. The data were converted to QCT format by processing with QCT Pro. The CT images were browsed at the coronal level, excluding images of thoracolumbar metal implants. The measurement process includes: (1) Analysis of the coronal screenshot of the reconstructed image of the T12-L2 three vertebral bodies, with browsing in three different dimensions and selection of any two of the T12-L2 vertebral bodies for placement sense. (2) The system automatically calculates the average bone mineral density of the two vertebral bodies while avoiding areas with severe bone hyperplasia, bone islands, and low-density areas running along the central groove of the vertebral body. (3) QCT-assessed

bone mineral density values are chosen as average spine bone mineral density values. According to previous studies and the applicability of the Chinese population, this study was based on the American College of Radiology's QCT diagnostic criteria, and a bone mineral density value less than 80 mg/cm³ was diagnosed as osteoporosis [9].

The European Spine Phantom (ESP No 145) was used to perform 10 repeated localization scans on Lightspeed VCT before the start of this study. The scan sequence was a low-dose chest CT lung cancer screening scan sequence. A QCT calibration phantom scan was performed after the scan. We ensured quality control by using the European cross-calibration of the spine phantom and the QCT calibration phantom.

Clinical and biochemical exam data

The attending physician of the oncology department consulted the clinical medical record system of our hospital to obtain information on patients with lung cancer.

We collected the patient's socio-demographic information, including age, sex, smoking (never, ever, now), alcohol consumption (never, ever, now), drug use, diabetes history, and chronic obstructive pulmonary disease. We also consulted the medical records to obtain the serum albumin and alkaline phosphatase levels of the lung cancer patients when they were diagnosed with lung cancer.

The treatment and follow-up of patients with lung cancer followed the global lung cancer guidelines. Regular imaging examinations were used to evaluate the curative effect during the treatment and follow-up. We evaluated the occurrence and location of bone metastases by routine imaging, including 99-Tc-MDP ECT/CT/MRI. We used ECT positivity as the diagnostic standard for bone metastasis. When CT or MRI showed bone destruction and there was no ECT examination, we invited two physicians with more than 15 years of experience in nuclear medicine for consultation. When the two nuclear medicine physicians agreed on a diagnosis of bone metastasis, we accepted that conclusion. The study outcome was defined as the progression to bone metastasis or the end of the follow-up period for patients with lung cancer. The time from the diagnosis of lung cancer to the occurrence of bone metastasis was recorded as the time of bone metastasis.

Statistics

The statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS), version 23.0. The descriptive analysis involved calculating the median and range (expressed as P50 (P25–P75)) for

quantitative data and frequency for qualitative variables (expressed as n (%)). We conducted the Kruskal–Wallis test on the sample, the Pearson Chi-square test was used to compare qualitative variables, and the Wilcoxon test was used for quantitative data. To study the risk factors for bone metastases in lung cancer patients, a univariate analysis was performed using Cox regression, followed by a multivariate analysis with the variables that achieved a ($P < 0.01$). The overall survival analysis was conducted using the Kaplan–Meier method, and the log-rank test was employed to compare survival between groups. A p -value of less than 0.05 is considered statistically significant. Survival analysis and forest plot drawing are completed using R version 4.1.1.

Ethical approval declarations

1. Approval: We received approval from the local ethics committee (Ethical Approval Number: 2021 Aaron trial Examination No. (68)).

2. Accordance: The study was conducted per the Declaration of Helsinki, and the methods were carried out in accordance with the relevant guidelines and regulations.

3. Informed consent: Since the study involved secondary analysis of existing imaging data from subjects, all participants were exempted from the requirement of providing informed consent in accordance with the ethical guidelines of the People's Hospital of Henan Province.

RESULTS

We recruited 400 lung cancer patients who underwent opportunistic screenings for osteoporosis using LDCT scans at the hospital Table 1. Seventy-four newly diagnosed lung cancer patients had osteoporosis, while the others did not. The clinical characteristics, including BMI, sex, smoking, drinking, diabetes mellitus, TNM Classification (pN), COPD, chemotherapy, and radiation therapy, were similar between the newly diagnosed lung cancer patients with and without osteoporosis (all $P > 0.05$). However, age was significantly higher in newly diagnosed lung cancer patients with osteoporosis than in freshly diagnosed lung cancer patients without osteoporosis ($P < 0.01$). There were differences between newly diagnosed lung cancer patients with and without osteoporosis in terms of serum albumin, surgery, and other therapies (all $P < 0.05$).

In the univariate analysis, factors such as other therapies, diabetes mellitus, surgery, serum albumin, and osteoporosis were significant for bone metastases (all $P < 0.05$). In multivariate analysis, surgery (HR 0.31, 95%CI 0.17–0.57, $P < 0.01$) and osteoporosis (HR 3.30, 95%CI 1.90–5.73, $P < 0.01$) were identified as significant

Table 1: Baseline Characteristics of Lung Cancer Patients with and Without Osteoporosis

Characteristics	Total (N)	Lung Cancer Without Osteoporosis (N=326)	Lung Cancer With Osteoporosis (N=74)	Test Statistic	P Value
Sex	400			$\chi^2 = 0.10$	0.752
Male	-	196/326 (60.12%)	43/74 (58.11%)		
Female	-	130/326 (39.88%)	31/74 (41.89%)		
Age, years	400			F=56.43	0.013
Median (IQR)	-	61.00 (54.00-64.08)	68.00 (65.00-71.08)		
Range	-	29.00-85.00	50.00-80.00		
BMI, kg/m2	400			F=0.58	0.45
Median (IQR)	-	23.40 (21.20-25.80)	23.05 (21.59-24.81)		
Range	-	13.80-34.80	13.70-33.40		
Smoking	400			$\chi^2 = 0.61$	0.742
Never	-	170/326 (52.15%)	40/74 (54.05%)		
Now	-	75/326 (23.01%)	14/74 (18.92%)		
Ever	-	81/326 (24.85%)	20/74 (27.03%)		
Drinking	400			$\chi^2 = 2.77$	0.252
Never	-	229/326 (70.25%)	59/74 (79.73%)		
Now	-	41/326 (12.58%)	7/74 (9.46%)		
Ever	-	56/326 (17.18%)	8/74 (10.81%)		
COPD	400			$\chi^2 = 0.54$	0.462
Yes	-	19/326 (5.83%)	6/74 (8.11%)		
No	-	307/326 (94.17%)	68/74 (91.89%)		
Diabetes Mellitus	400			$\chi^2 = 3.16$	0.082
Yes	-	30/326 (9.20%)	12/74 (16.22%)		
No	-	296/326 (90.80%)	62/74 (83.78%)		
Alkaline Phosphatase, U/L	400			$\chi^2 = 1.93$	0.17
< 125	-	309/326 (94.79%)	67/74 (90.54%)		
≥ 125	-	17/326 (5.21%)	7/74 (9.46%)		
Serum Albumin, g/L	400			$\chi^2 = 5.78$	0.022
≤ 35	-	110/326 (33.74%)	36/74 (48.65%)		
> 35	-	216/326 (66.26%)	38/74 (51.35%)		
TNM Classification (pN)	400			$\chi^2 = 4.83$	0.182
pN1	-	74/326 (22.70%)	14/74 (18.92%)		
pN2	-	91/326 (27.91%)	14/74 (18.92%)		
pN3	-	150/326 (46.01%)	38/74 (51.35%)		
pN4	-	11/326 (3.37%)	6/74 (8.11%)		
Surgery	400			$\chi^2 = 17.22$	< 0.012
Yes	-	232/326 (71.17%)	34/74 (45.95%)		
No	-	94/326 (28.83%)	40/74 (54.05%)		
Chemotherapy	400			$\chi^2 = 0.20$	0.662
Yes	-	288/326 (88.34%)	64/74 (86.49%)		
No	-	38/326 (11.66%)	10/74 (13.51%)		
Radiation Therapy	400			$\chi^2 = 0.77$	0.382
Yes	-	43/326 (13.19%)	7/74 (9.46%)		
No	-	283/326 (86.81%)	67/74 (90.54%)		
Other Therapy	400			$\chi^2 = 11.53$	< 0.012
Yes	-	35/326 (10.74%)	19/74 (25.68%)		
No	-	291/326 (89.26%)	55/74 (74.32%)		

Note: BMI = Body Mass Index; COPD = Chronic Obstructive Pulmonary Disease; TNM = Tumor-Node-Metastasis; All unlabeled test statistics are χ^2 values.

prognostic factors for bone metastases Table 2. Univariate and multivariate COX regression forest plots for bone metastasis in patients with lung cancer are presented in Figure 2.

At the end of the study, 59 (14.75%) patients with lung cancer developed bone metastases, with a median survival time of 56 months (95% CI 49-NA). Compared with those without osteoporosis in newly diagnosed lung cancer patients, those with osteoporosis in newly diagnosed lung cancer could quickly develop bone metastases (median time to bone metastasis development, 35 months; 95% CI, 26- NA months vs. 56 months; 95% CI, 56- NA; $P < 0.01$). Compared with those without surgery treatment in lung cancer patients, those with surgery treatment had a delayed time to develop bone metastases (median time to bone metastasis development, 44 months; 95% CI, 31- NA months vs 56 months; 95% CI, 49- NA; $P < 0.01$; Table 3 and Figure 2.

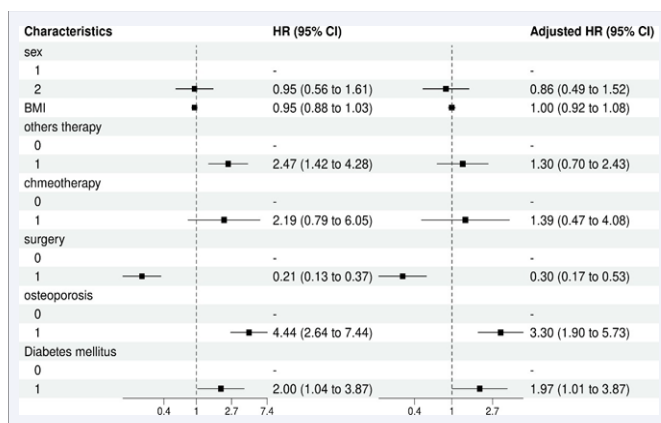


Figure 2 Univariate and multivariate COX regression forest plots for bone metastasis in lung cancer patients.

DISCUSSION

Lung cancer exhibits a high propensity for osteolytic bone metastasis, with its key progression process divided into three sequential stages: tumor invasion, tumor cell migration, and bone tissue colonization [10]. These stages are tightly regulated by multiple factors, including the receptor activator of nuclear factor B (RANK)/RANK ligand (RANKL)/osteoprotegerin (OPG) pathway, specific exosome subsets, and bone morphogenetic protein 2 (BMP2) [10-13]. Notably, the RANK/RANKL/OPG pathway is a shared signaling axis between lung cancer bone metastasis and osteoporosis pathogenesis. Specifically, the binding of RANK (expressed on osteoclast precursors) to its ligand RANKL (secreted by tumor or stromal cells) promotes osteoclast differentiation and activation; in contrast, OPG an endogenous decoy receptorsuppresses osteoclast activity by competitively binding to RANKL. An elevated RANKL: OPG ratio correlates with increased metastatic potential of lung cancer cells. Furthermore, the prevention or treatment of bone metastasis-related skeletal events (BMREs) has been shown to exacerbate osteoporosis progression in affected patients [14].

Trabecular vBMD can be acquired using low-dose chest CT scan data combined with QCT technology. The

Table 3: Comparisons of Time to Bone Metastasis Survival Data Among Lung Cancer Patients Stratified by Surgery and Osteoporosis

Variables	No. of lung cancer patients	Survival, median (95%CI), months	P
Surgery			
Yes	266 22(8.27)	56(49 - NA)	<0.01
No	134 37 (27.61)	44 (31 - NA)	
Osteoporosis			
	74 27 (36.49)	35 (26 - NA)	<0.01
	326 32 (9.82)	56 (56 - NA)	

Table 2: Univariate and Multivariate Cox Regression for Prognostic Risk of Lung Cancer Progression to Bone Metastases

Characteristic	Univariable			Multivariable		
	HR	95%CI	P value	HR	95%CI	P value
Age	1.01	0.98C1.03	0.642	0.97	0.94C1.00	0.04
Others therapy						
No	2.47	1.42C4.28	<0.01	1.30	0.70C2.43	0.408
Yes						
Surgery						
No	0.21	0.12C0.36	<0.01	0.31	0.17C0.57	<0.01
Yes						
Osteoporosis						
No	4.44	2.64C7.44	<0.01	3.30	1.90C5.73	<0.01
Yes						
Serum albumin						
No	0.36	0.21C0.61	<0.01	0.60	0.34C1.07	0.081
Yes						
Diabetes mellitus						
No	2.00	1.03C3.86	0.039	1.81	0.92C3.57	0.087
Yes						

HR = Hazard Ratio; CI = Confidence Interval. Reference group (No) is marked with "".

examination is convenient and rapid, with no additional ionizing radiation being necessary. Cheng et al. [8], were the first to demonstrate the feasibility of measuring trabecular bone mineral density in the Chinese population using low-dose chest CT. Opportunistic osteoporosis screening via low-dose chest CT has a higher detection rate of osteoporosis in the elderly than the traditional DXA, exhibiting higher sensitivity [15,16].

The prevalence of osteoporosis in lung cancer patients at the time of diagnosis is 18.5%, which is comparable to that of the general population in China, indicating relatively good bone health status before cancer diagnosis [17]. Zhou et al. [18], showed that lung cancer patients with a history of smoking and COPD have lower bone density compared to those without these risk factors. The baseline data of this study indicated that there was no statistically significant disparity in the smoking status among lung cancer patients with and without osteoporosis. This might be ascribed to the fact that the data were derived from the opportunistic lung cancer screening database of health examinations, and the patients might be unaware of or not diagnosed with COPD. Bari et al. [19], proposed that COPD is an independent risk factor for osteoporosis in men and has no significant correlation with smoking history, which is contrary to the study of Zhou et al. [18]. Pompe et al. [20], revealed that current smokers had the fastest bone mineral density decline within 3 years. We will concentrate on the longitudinal relationship between smoking history and the alteration of bone mass in lung cancer patients in future studies.

Our findings demonstrate that bone density loss, identified via low-dose chest computed tomography (CT) screening at the time of lung cancer diagnosis, serves as an independent risk factor for lung cancer bone metastasis. Specifically, compared with patients without bone density loss, those with bone density loss exhibit accelerated progression to lung cancer bone metastasis. This observation is consistent with the findings reported by Lee et al. [21]. However, a large clinical study by Chen et al. [22], has shown that the presence of bone density loss at the time of breast cancer diagnosis is not correlated with bone metastasis; rather, it only accelerates the process of breast cancer bone metastasis. This difference may be attributed to variances in mechanisms underlying breast and lung cancer metastasis.

The primary tumor orchestrates the microenvironment within bones and establishes conditions for dormancy and dissemination of tumor cells, ultimately leading to multi-organ metastases and mortality [23]. Breast cancer cells have already disseminated throughout the body upon

detection at their primary site, remaining dormant to evade treatment while external factors such as inflammation and aging heighten their risk of recurrence and accelerate osteoporosis progression [24]. In contrast, lung cancer metastasis occurs following the completion of invasion and migration, with tumor cells entering a dormant state within marrow cell microenvironments [25]; here, they interact with various marrow cells, causing adaptive changes while also directly or indirectly promoting lung cancer bone metastasis through these interactions [26,27]. Therefore, we propose that once bone (a common metastatic site for lung cancer) is identified as a target, the bone marrow cellular microenvironment provides a fertile "soil" for migrating tumor cells ("seeds") suggesting that lung cancers metastatic pattern aligns more closely with the "seed"-soil theory (SST) than that of breast cancer. Our study provides clinical evidence supporting this SST-related mechanism during tumor metastasis. In future studies, we will further investigate two key directions: 1) the impact of osteoporosis treatment on lung cancer bone metastasis (LCBM); and 2) the potential role of osteoporosis treatment in the prevention and management of LCBM. We also observed that surgical treatment served as a protective factor against bone metastasis in lung cancer and prolonged the median time for lung cancer to progress to bone metastasis. Whether it was lobectomy, sublobar resection, or pneumonectomy, these procedures represent valuable and effective measures for enhancing the long-term survival rate of lung cancer patients [28-30]. Nevertheless, according to the report, 30-70% of non-small cell lung cancer patients still encountered recurrence following complete resection, including distant metastasis [31]. This phenomenon is associated with achieving pathological remission through lung cancer treatment, with those failing to achieve such remission exhibiting a heightened risk of bone metastasis [32]. For lung cancer patients unable to undergo immediate surgical intervention upon diagnosis, receiving preoperative neoadjuvant immunotherapy combined with chemotherapy can reduce staging and enhance survival rates and quality of life by increasing post-surgery pathological remission [33,34]. Hence, the added benefit of surgical intervention in the management of lung cancer is underscored as a protective factor against bone metastasis, thereby potentially slowing its progression.

The study had the following limitations. First, there was an age and sex bias in patient inclusion. The elderly and men accounted for most of the patients with lung cancer. Second, LDCT lung cancer screening is capable of sensitively detecting a higher number of early-stage lung cancer patients. The study primarily involved patients in

the early to midstages of lung cancer. Third, in the bone mineral density measurement, severe bone hyperplasia, and larger bone island, we chose the T12/L1 vertebral body bone mineral density value as the final spine QCT bone mineral density value.

CONCLUSION

In conclusion, the newly diagnosed lung cancer with osteoporosis was associated with a risk of bone metastasis and accelerated progression of bone metastasis. Surgery is considered a protective factor against bone metastasis in lung cancer. Our findings highlight the need for early identification of osteoporosis among newly diagnosed lung cancer patients to improve the prognosis of cancer patients with de novo bone metastases.

REFERENCES

- Coleman RE. Metastatic bone disease: clinical features, pathophysiology and treatment strategies. *Cancer Treat Rev*. 2001; 27: 165-176.
- Hong S, Youk T, Lee SJ, Kim KM, Vajdic CM. Bone metastasis and skeletal-related events in patients with solid cancer: A Korean nationwide health insurance database study. *PLoS One*. 2020; 15: e0234927.
- Paget S. The distribution of secondary growths in cancer of the breast. 1889. *Cancer Metastasis Rev*. 1989; 8: 98-101.
- Tu SM, Lin SH. Current trials using bone-targeting agents in prostate cancer. *Cancer J*. 2008; 14: 35-39.
- Fernández Vallone VB, Hofer EL, Choi H, Bordenave RH, Batagelj E, Feldman L, et al. Behaviour of mesenchymal stem cells from bone marrow of untreated advanced breast and lung cancer patients without bone osteolytic metastasis. *Clin Exp Metastasis*. 2013; 30: 317-332.
- Aaron N, Costa S, Rosen CJ, Qiang L. The Implications of Bone Marrow Adipose Tissue on Inflammation. *Front Endocrinol (Lausanne)*. 2022; 13: 853765.
- Martel D, Monga A, Chang G. Osteoporosis Imaging. *Radiol Clin North Am*. 2022; 60: 537-545.
- Cheng X, Zhao K, Zha X, Du X, Li Y, Chen S, et al; China Health Big Data (China Biobank) project investigators. Opportunistic Screening Using Low-Dose CT and the Prevalence of Osteoporosis in China: A Nationwide, Multicenter Study. *J Bone Miner Res*. 2021; 36: 427-435.
- Engelke K, Adams JE, Armbrrecht G, Augat P, Bogado CE, Bouxsein ML, et al. Clinical use of quantitative computed tomography and peripheral quantitative computed tomography in the management of osteoporosis in adults: the 2007 ISCD Official Positions. *J Clin Densitom*. 2008; 11: 123-162.
- Xue M, Ma L, Zhang P, Yang H, Wang Z. New insights into non-small cell lung cancer bone metastasis: mechanisms and therapies. *Int J Biol Sci*. 2024; 20: 5747-5763.
- The PLOS ONE Editors. Retraction: Differential Expression of the RANKL/RANK/OPG System Is Associated with Bone Metastasis in Human Non-Small Cell Lung Cancer. *PLoS ONE*. 2024; 19: e0314046.
- Hoshino A, Costa-Silva B, Shen TL, Rodrigues G, Hashimoto A, Tesic Mark M, et al. Tumour exosome integrins determine organotropic metastasis. *Nature*. 2015; 527: 329-335.
- Huang F, Cao Y, Wu G, Chen J, Wang C, Lin W, et al. BMP2 signalling activation enhances bone metastases of non-small cell lung cancer. *J Cell Mol Med*. 2020; 24: 10768-10784.
- Peng X, Guo W, Ren T, Lou Z, Lu X, Zhang S, et al. Differential expression of the RANKL/RANK/OPG system is associated with bone metastasis in human non-small cell lung cancer. *PLoS One*. 2013; 8: e58361.
- Xu XM, Li N, Li K, Li XY, Zhang P, Xuan YJ, et al. Discordance in diagnosis of osteoporosis by quantitative computed tomography and dual-energy X-ray absorptiometry in Chinese elderly men. *J Orthop Translat*. 2018; 18: 59-64.
- Li N, Li XM, Xu L, Sun WJ, Cheng XG, Tian W. Comparison of QCT and DXA: Osteoporosis Detection Rates in Postmenopausal Women. *Int J Endocrinol*. 2013; 2013: 895474.
- Xiao PL, Cui AY, Hsu CJ, Peng R, Jiang N, Xu XH, et al. Global, regional prevalence, and risk factors of osteoporosis according to the World Health Organization diagnostic criteria: a systematic review and meta-analysis. *Osteoporos Int*. 2022; 33: 2137-2153.
- Zhou Y, Hu Y, Yan X, Zheng Y, Liu S, Yao H. Smoking index and COPD duration as potential risk factors for development of osteoporosis in patients with non-small cell lung cancer - A retrospective case control study evaluated by CT Hounsfield unit. *Heliyon*. 2023; 9: e20885.
- Bari MZJ, Patwary I, Hussain D, Islam SAHMM, Rasker JJ. Association of COPD with osteoporosis in male smokers: A case control study in a tertiary medical college hospital in Bangladesh. *J Back Musculoskelet Rehabil*. 2020; 33: 119-125.
- Pompe E, Bartstra J, Verhaar HJ, de Koning HJ, van der Aalst CM, Oudkerk M, et al. Bone density loss on computed tomography at 3-year follow-up in current compared to former male smokers. *Eur J Radiol*. 2017; 89: 177-181.
- Lee S, Kim YG, Jung HI, Lim JS, Nam KC, Choi HS, et al. Bone-on-a-chip simulating bone metastasis in osteoporosis. *Biofabrication*. 2024; 16.
- Chen HM, Chen FP, Yang KC, Yuan SS. Association of Bone Metastasis with Early-Stage Breast Cancer in Women With and Without Precancer Osteoporosis According to Osteoporosis Therapy Status. *JAMA Netw Open*. 2019; 2: e190429.
- Ji X, Bei HP, Zhong G, Shao H, He X, Qian X, et al. Premetastatic Niche Mimicking Bone-On-A-Chip: A Microfluidic Platform to Study Bone Metastasis in Cancer Patients. *Small*. 2023; 19: e2207606.
- Wieder R. Awakening of Dormant Breast Cancer Cells in the Bone Marrow. *Cancers (Basel)*. 2023; 15: 3021.
- Mohme M, Riethdorf S, Pantel K. Circulating and disseminated tumour cells - mechanisms of immune surveillance and escape. *Nat Rev Clin Oncol*. 2017; 14: 155-167.
- Zhang X. Interactions between cancer cells and bone microenvironment promote bone metastasis in prostate cancer. *Cancer Commun (Lond)*. 2019; 39: 76.
- Li J, Wu J, Xie Y, Yu X. Bone marrow adipocytes and lung cancer bone metastasis: unraveling the role of adipokines in the tumor microenvironment. *Front Oncol*. 2024; 14: 1360471.
- Gu C, Wang R, Pan X, Huang Q, Zhang Y, Yang J, et al. Sublobar resection versus lobectomy in patients aged ≤35 years with stage IA non-small cell lung cancer: a SEER database analysis. *J Cancer Res Clin Oncol*. 2017; 143: 2375-2382.
- Gu C, Huang Z, Dai C, Wang Y, Ren Y, She Y, et al. Prognostic Analysis of Limited Resection Versus Lobectomy in Stage IA Small Cell Lung Cancer Patients Based on the Surveillance, Epidemiology, and End Results Registry Database. *Front Genet*. 2018; 9: 568.
- Gu C, Wang R, Pan X, Huang Q, Luo J, Zheng J, et al. Comprehensive study

- of prognostic risk factors of patients underwent pneumonectomy. *J Cancer*. 2017; 8: 2097-2103.
31. Yuan Y, Huang Q, Gu C, Chen H. Disease-free survival improved by use of adjuvant EGFR tyrosine kinase inhibitors in resectable non-small cell lung cancer: an updated meta-analysis. *J Thorac Dis*. 2017; 9: 5314-5321.
 32. Bao Y, Gu C, Xie H, Zhao S, Xie D, Chen C, et al. Comprehensive study of neoadjuvant targeted therapy for resectable non-small cell lung cancer. *Ann Transl Med*. 2021; 9: 493.
 33. Ma D, Xu Y, Qin Y, Li S, Li J, Jiang Y, et al. Neoadjuvant immunotherapy followed by surgery with curative intent in 35 patients with advanced NSCLC: the retrospective experiences of a multidisciplinary team. *Ann Transl Med*. 2022; 10: 609.
 34. Faehling M, Witte H, Sebastian M, Ulmer M, Sätzler R, Steinestel K, et al. Real-world multicentre analysis of neoadjuvant immunotherapy and chemotherapy in localized or oligometastatic non-small cell lung cancer (KOMPASSneoOP). *Ther Adv Med Oncol*. 2022; 14: 17588359221085333.