ORIGINAL ARTICLE

Clinical study on SUVmax combined with ALP, N-MID, TPINP and BMD in the early diagnosis of lung cancer bone metastasis

Hong Gu*[1], Guowei Tan[2], Qinghe Yu[3]

[1] *Department of Nuclear Medicine, Baogang Hospital, Baotou, Inner Mongolia, China*
[2] *Department of Nuclear Medicine, Qilu Hospital of Shandong University, Jinan, Shandong, China*
[3] *Department of Ultrasound Medicine, Shandong Electric Power Center Hospital, Jinan, Shandong, China*

Received: May 3, 2025 **Accepted:** July 30, 2025 **Online Published:** December 31, 2025
DOI: 10.5430/dcc.v11n2p19 **URL:** https://doi.org/10.5430/dcc.v11n2p19

ABSTRACT

Objective: In combination with Maximum Standardized Uptake Value (SUVmax) from SPECT/CT scans in lung cancer patients, serum alkaline phosphatase (ALP), molecular fragments in the N end of osteocalcin (N-MID), total procollagen type 1 N-terminal propeptide (TPINP), and bone mineral density (BMD) measurements to explore the clinical early diagnosis of lung cancer bone metastasis.

Methods: A total of 107 patients diagnosed as lung cancer at a tertiary-level Class A hospital between January 2021 and June 2022 were enrolled, comprising 37 cases with bone metastasis and 70 cases without bone metastasis. All patients underwent relevant examinations. SPECT/CT was performed in the supine position with anterior and posterior whole-body bone imaging, using a matrix of 256 $\times$ 1,024, an energy peak of 140 keV, and a window width of 20%. SUVmax was measured. BMD measurement utilizes dual-energy X-ray absorptiometry to assess the first to fourth lumbar vertebrae, bilateral femoral necks, and total hip joints in the examinees, yielding bone mineral content per unit area (g/cm^2). Fasting blood samples in the morning were taken and a fully automated biochemical analyzer was used to measure ALP levels, and a fully automated chemiluminescence immunoassay analyzer was used to measure serum N-MID and TPINP levels.

Results: Patients with bone metastasis exhibited ALP, N-MID and TPINP levels of 120.30 $\pm$ 33.32 U/L, 19.03 $\pm$ 3.54 mg/L and 82.21 $\pm$ 26.65 mg/L, respectively, significantly higher than those in patients without bone metastasis (94.43 $\pm$ 30.30 U/L, 15.50 $\pm$ 4.01 mg/L, 55.58 $\pm$ 21.01 mg/L), $p < .001$, indicating a significant difference; The lumbar spine BMD in patients with bone metastasis was 0.82 $\pm$ 0.12 g/cm^2, compared to 0.89 $\pm$ 0.14 g/cm^2 in patients without bone metastasis, $p = .011$, demonstrating a statistical significance. Comparisons between patients with and without bone metastasis revealed no statistically significant differences in gender, pathological type, femoral neck BMD, or whole-body BMD ($p > .05$). The SUVmax value for adenocarcinoma patients was 11.45 $\pm$ 1.98, significantly lower than 13.51 $\pm$ 2.00 for patients with squamous cell carcinoma and 13.98 $\pm$ 2.02 for other types ($p < .001$), representing a statistically significant difference. For patients with tumors with diameter > 5 cm and TNM stage III–IV, SUVmax values were 13.38 $\pm$ 1.95 and 12.99 $\pm$ 2.00, respectively, significantly higher than those with tumors $\leq$ 5 cm (11.50 $\pm$ 2.01) and TNM stage I–II (11.77 $\pm$ 1.93), with $p < .001$ and $p = .002$, respectively, demonstrating a statistical significance. Comparison in SUVmax of gender and age showed $p > .05$, indicating no statistically significant difference. In patients with TNM stage III–IV, ALP, N-MID and TPINP levels were 110.39 $\pm$ 21.12 U/L, 18.62 $\pm$ 2.22 mg/L and 70.31 $\pm$ 17.02 mg/L, respectively, significantly higher than those in patients with TNM stage I–II (97.45 $\pm$ 19.82,

*Correspondence: Hong Gu; Email: guhong688@163.com; Address: Department of Nuclear Medicine, Baogang Hospital, Baotou, Inner Mongolia, 014010, China.

15.12 ± 2.14 and 60.12 ± 15.65, respectively. The corresponding p values were .001, < .001 and .002, indicating a statistical significance. Comparison in ALP, N-MID and TPINP levels among patients of different genders, ages, pathological types and tumor diameters showed p > .05, indicating no statistically significant differences. The areas under the ROC curves for ALP, N-MID and TPINP in the diagnosis of bone metastasis were 0.695, 0.734 and 0.837, respectively, with p < .05.
Conclusions: Serum ALP, N-MID and TPINP levels were significantly elevated in patients with bone metastasis of lung cancer in comparison to those without bone metastasis, while SUVmax showed no significant difference. SUVmax, ALP, N-MID and TPINP are associated with certain clinical and pathological characteristics in lung cancer patients. Among these, ALP, N-MID and TPINP demonstrate a potential diagnostic value for detecting bone metastasis in lung cancer.

Key Words: Lung cancer, Bone metastasis, Single photon emission computed tomography, Maximum standardized uptake value, Alkaline phosphatase, N-MID Osteocalcin, Total procollagen type 1 N-terminal propeptide

1. INTRODUCTION

Lung cancer is one of the most common malignant tumors, with persistently high incidence and mortality rates. Non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer cases, with a five-year survival rate of about 17.1%.[1] NSCLC frequently metastasizes to bones, brain, other lung regions and liver, with bone metastasis accounting for approximately 30%-40% of all lung cancer metastasis.[2] Pathological fractures caused by lung cancer bone metastasis, whether impending or actual, represent a difficult and challenging complication that impacts the prognosis of lung cancer patients, diminishes their quality of life, and may even be life-threatening.[3] Clinically, the diagnostic methods for lung cancer bone metastasis recommended by guidelines primarily rely on imaging examination results. According to relevant statistics, approximately 70% of patients with lung cancer are often diagnosed at the intermediate or advanced stages of bone metastasis, having already lost the opportunity for curative lung cancer surgery.[4] Currently, there are few clinically effective methods for predicting bone metastasis in lung cancer. Studies indicate that various types of molecules, host cells, and the extracellular microenvironment participate in the interactions of cancer cells during lung cancer bone metastasis, including osteoclast-mediated bone resorption and osteoblast-mediated bone formation.[5] Therefore, we speculate that biochemical bone metastasis likely occurs prior to imaging bone metastasis. To further enhance the prediction, diagnosis, and disease monitoring of lung cancer bone metastasis, this study aims to conduct a combined analysis of SPECT/CT maximum standardized uptake value (SUVmax) with existing biochemical markers of bone metabolism: serum alkaline phosphatase (ALP), molecular fragments in the N end of osteocalcin (N-MID) and bone mineral density (BMD). This integrated approach seeks to provide a robust theoretical foundation for clinical prediction, diagnosis, and treatment monitoring of bone metastasis.

2. DATA AND METHODS

2.1 General information

A total of 107 patients diagnosed with lung cancer at a tertiary-level Class A hospital between January 2021 and June 2022 were enrolled. The cohort comprised 63 males and 44 females. Forty-eight patients were aged < 60 years, while 59 patients were aged ≥ 60 years. Among them, 37 patients had bone metastasis from lung cancer, and 70 patients did not have bone metastasis.

Inclusion criteria are listed as follows: (1) Pathologically or cytologically confirmed lung cancer: characterized by irregular cell morphology, small nuclei, etc.; bone metastasis demonstrated by imaging studies[6] showing multiple patchy or cotton-ball-like lesions, diffuse high-density shadows with indistinct borders; (2) Karnofsky Performance Status (KPS) ≥ 70 points;[7] (3) No prior radiotherapy or chemotherapy before enrollment; (4) Informed consent obtained from both the patients and family members.

Exclusion criteria are listed as follows: (1) History of osteoarthritis, rheumatoid arthritis, or other bone metabolic disorders; (2) Use of medications affecting bone metabolism (e.g., corticosteroids, bisphosphonates) within the past 6 months; (3) Traumatic fracture within the past year; (4) Individuals with psychiatric disorders or communication impairments.

2.2 Experimental methods

2 mL of fasting blood from each patient were collected in the morning, and then centrifuged at 2,000 rpm for 10 minutes at low temperature, and the collected serum were immediately stored at -80°C in the refrigerator, ALP levels were measured by use of Olympus AU5400 automated biochemical analyzer, serum N-MID and total procollagen type 1 N-terminal propeptide (TPINP) levels were detected by an automated chemiluminescent immunoassay analyzer.

Bone Density Testing: Bone density (g/cm^2) was measured by using dual-energy X-ray absorptiometry (DXA) at the first to fourth lumbar vertebrae, both femoral necks, and the entire hip joint. BMD refers to the bone mineral content per unit area in g/cm^2, with the precise value expressed to three decimal places. The testing instrument was Lunar DXA bone densitometer manufactured by GE Healthcare, recognized by World Health Organization (WHO) as the gold standard for diagnosing BMD and osteoporosis.

2.3 SPECT/CT examinations

The new GE Infinia VC Hawkeye PET/CT system, featuring a low-energy high-resolution collimator, was employed in this study. The radiotracer 99mTc-MDP was supplied by the China Institute of Atomic Energy, with a radiochemical purity of > 95%. The patient received an intravenous injection of 25 mCi of ^{99m}Tc-labeled methylene diphosphonate (MDP). After drinking 500 mL of water, the patient was instructed to empty the bladder 3-4 hours later. The patient was positioned supine for anterior and posterior whole-body bone scintigraphy. The matrix was 256 × 1,024, the energy peak was 140 keV, and the window width was 20%. Analgesics were administered to patients experiencing severe pain, and local static bone scintigraphy were conducted when necessary.

2.4 Statistical treatment

SPSS 20.0 statistical software was applied to the statistical analysis. The measurement data included SUVmax, ALP, N-MID and TPINP, etc., presented as ($\bar{x}\pm$s). Independent sample t-tests were used to analyze the differences between two groups, while the analysis of variance (ANOVA) was used to assess the differences among multiple groups. Categorical data, including gender, were expressed as n (%). Differences between groups were analyzed using chi-square (χ^2) tests. Diagnostic value was assessed using receiver operating characteristic (ROC) curve analysis. Inter-group comparisons with $p < .05$ were considered statistically significant.

3. RESULTS

3.1 Comparison of clinical data between lung cancer patients with and without bone metastasis

Patients with lung cancer bone metastasis exhibited significantly higher levels of ALP, N-MID, and TPINP in comparison to those without bone metastasis ($p < .05$), while their lumbar spine BMD was significantly lower than that in patients without bone metastasis ($p < .05$). No statistically significant differences were observed between bone metastasis and non-metastatic patients in terms of gender, pathological type, or other characteristics ($p > .05$) (see Tables 1-4).

Table 1. Comparison of general information between bone metastasis and bone metastasis patients [$\bar{x}\pm$s, n (%)]

Markers		Bone Metastasis (n = 37)	Non-metastasis (n = 70)	t/χ^2	p
Gender	Male	22 (59.46)	41 (58.57)	0.008	.929
	Female	15 (40.54)	29 (41.43)		
Age (years old)		62.20±8.21	63.54±9.03	-0.753	.453

Table 2. Comparison of pathological type between bone metastasis and bone metastasis patients [n (%)]

Type	Bone Metastasis (n = 37)	Non-metastasis (n = 70)	t/χ^2	p
Adenocarcinoma	20 (54.05)	39 (55.71)		
Squamous cell carcinoma	12 (32.43)	22 (31.43)	0.028	.986
Others	5 (13.51)	9 (12.86)		

Table 3. Comparison of SUVmax, ALP, N-MID and TPINP between bone metastasis and bone metastasis patients ($\bar{x}\pm$s)

Markers	Bone Metastasis (n = 37)	Non-metastasis (n = 70)	t/χ^2	p
SUVmax	12.57±2.10	12.20±2.03	0.886	.378
ALP (U/L)	120.30±33.32	94.43±30.30	4.058	< .001
N-MID (mg/L)	19.03±3.54	15.50±4.01	4.505	< .001
TPINP (mg/L)	82.21±26.65	55.58±21.01	5.672	< .001

Table 4. Comparison of BMD between bone metastasis and bone metastasis patients ($\bar{x}\pm$s)

Markers (g/cm^2)	Bone Metastasis (n = 37)	Non-metastasis (n = 70)	t/χ^2	p
Lumbar spine BMD	0.82±0.12	0.89±0.14	-2.580	.011
Neck of femur BMD	0.76±0.11	0.80±0.13	-1.593	.114
Whole body BMD	0.70±0.14	0.72±0.12	-0.774	.441

3.2 Relationship between SUVmax and clinical pathological characteristics in patients

Patients with adenocarcinoma exhibited significantly lower SUVmax values in comparison to those with squamous cell carcinoma and other types ($p < .05$). Patients with tumors > 5 cm in diameter and TNM stage III–IV demonstrated significantly higher SUVmax values than those with tumors $\leq$ 5 cm in diameter and TNM stage I–II ($p < .05$) (see Tables 5-9).

Table 5. Relationship between SUVmax and gender ($\bar{x}\pm$s)

Gender	n	SUVmax	t/F	p
Male	63	12.43±2.03	0.618	.538
Female	44	12.18±2.10		

Table 6. Relationship of SUVmax with age ($\bar{x}\pm$s)

Age (years old)	n	SUVmax	t/F	p
< 60	48	12.30±2.12	-0.123	.902
≥ 60	59	12.35±2.07		

Table 7. Relationship of SUVmax with pathological type ($\bar{x}\pm$s)

Pathological Type	n	SUVmax	t/F	p
Adenocarcinoma	59	11.45±1.98		
Squamous cell carcinoma	34	13.51±2.00a	16.385	< .001
Others	14	13.98±2.02a		

Table 8. Relationship of SUVmax with tumor diameter in patients ($\bar{x}\pm$s)

Tumor diameter	n	SUVmax	t/F	p
≤ 5 cm	60	11.50±2.01	-4.865	< .001
> 5 cm	47	13.38±1.95		

Table 9. Relationship of SUVmax with tumor TNM staging in patients ($\bar{x}\pm$s)

TNM stage	n	SUVmax	t/F	p
I–II	58	11.77±1.93	-3.204	.002
III–IV	49	12.99±2.00		

Table 10. Relationship of ALP, N-MID and TPINP with gender ($\bar{x}\pm$s)

Gender	n	ALP (U/L)	N-MID (mg/L)	TPINP (mg/L)
Male	63	104.43±19.92	16.92±2.10	63.45±16.65
Female	44	101.87±20.04	16.44±2.19	66.71±17.02
t		0.653	1.143	-0.988
p		.516	.256	.326

3.3 Relationship of ALP, N-MID and TPINP with clinical-pathological characteristics in patients

Patients with TNM stage III–IV showed significantly higher levels of ALP, N-MID and TPINP in comparison to those with TNM stage I–II ($p < .05$). There were no statistically significant differences in ALP, N-MID and TPINP among patients of different genders, ages, pathological types and tumor diameters ($p > .05$) (see Tables 10-14).

3.4 The value of ALP, N-MID and other markers in diagnosing bone metastasis

Pathological examination serves as the gold standard for diagnosing bone metastasis. The areas under the ROC curves for ALP, N-MID and TPINP in diagnosing bone metastasis were 0.695, 0.734 and 0.837, respectively, with $p < .05$. The area under the curve (95% CI) for lumbar spine BMD was 0.587 (0.470–0.704), $p = .139$, indicating no statistically significant diagnostic value for bone metastasis. Specific parameters are shown in Table 15.

4. Discussion

Patients with bone metastasis frequently suffer from bone pain and skeletal-related events (SREs), including pathological fractures and spinal cord compression. The optimal treatment aims to delay the progression of bone metastasis, alleviate pain, prevent SREs and improve quality of life. It is difficult to assess the objective response of metastatic bone lesions to systemic therapies such as endocrine and cytotoxic treatments.[7] X-ray examination is the most convenient and

economical routine method for bone assessment. However, it is not sensitive to small bone metastasis measuring less than 1 cm. While osteolytic or mixed osteolytic-osteoblastic bone metastasis can be measured and quantified via CT and MRI, osteoblastic metastasis cannot be detected by these imaging modalities.[8] Bone scans are a representative imaging modality for diagnosing and evaluating bone abnormalities, including bone metastasis, and assessing treatment response. However, the diagnosis of bone metastasis is primarily based on the macroscopic assessment, which can only identify the location, size, shape, and number on imaging studies, and relies heavily on the physician's experience.[9] Although this is a highly useful method, the diagnostic capability of whole-body imaging is generally considered inferior to SPECT. SPECT can reveal dense phenomena in bone trauma, inflammation, degeneration, and other lesions, which may be misdiagnosed as cancerous bone metastasis, leading to false positive results.[10] The initial stage of bone metastasis exhibits only limited skeletal anatomical changes, which can be detected using SPECT/CT. SPECT/CT has been demonstrated to enhance the specificity and positive predictive value of bone scans, offering diagnostic value beyond conventional bone imaging.[11] This study found that lumbar spine BMD was significantly lower in patients with bone metastasis in comparison to those without bone metastasis ($p < .05$), while no significant differences were observed in femoral neck BMD or whole-body BMD. Evidence indicates that bone metastasis is associated with significant bone resorption and bone loss, with the lumbar spine potentially being more susceptible to bone metastasis. This may be related to certain osteolytic substances produced by tumor cells, such as prostaglandins, which can activate osteoclasts and increase bone resorption. Because the lumbar spine is located along the longitudinal axis of human body and plays a role in significant daily activities, it has a relatively rich blood supply, increasing the likelihood of bone metastasis.

Table 11. Relationship of ALP, N-MID and TPINP with age ($\bar{x}\pm$s)

Age (years old)	*n*	ALP (U/L)	N-MID (mg/L)	TPINP (mg/L)
≥ 60	48	103.34±21.19	16.71±2.18	65.10±15.58
< 60	59	103.40±22.25	16.73±2.24	64.54±17.21
t		-0.014	-0.046	0.175
p		.989	.963	.862

Table 12. Relationship of ALP, N-MID and TPINP with pathological type ($\bar{x}\pm$s)

Pathological Type	*n*	ALP (U/L)	N-MID (mg/L)	TPINP (mg/L)
Adenocarcinoma	59	104.45±22.38	16.68±2.40	66.64±20.10
Squamous cell carcinoma	34	102.32±21.18	16.28±2.35	61.19±21.16
Others	14	101.41±22.09	17.96±2.46	65.73±20.45
F		0.167	2.465	0.780
p		.847	.090	.461

Table 13. Relationship of ALP, N-MID and TPINP with tumor diameter ($\bar{x}\pm$s)

Tumor diameter	*n*	ALP (U/L)	N-MID (mg/L)	TPINP (mg/L)
≤ 5 cm	60	104.13±20.29	16.45±2.19	63.49±18.38
> 5 cm	47	102.41±21.14	17.07±2.23	66.45±17.10
t		0.427	-1.442	-0.852
p		.670	.152	.396

Table 14. Relationship of ALP, N-MID and TPINP and TNM staging ($\bar{x}\pm$s)

TNM stage	*n*	ALP (U/L)	N-MID (mg/L)	TPINP (mg/L)
I–II	58	97.45±19.82	15.12±2.14	60.12±15.65
III–IV	49	110.39±21.12	18.62±2.22	70.31±17.02
t		-3.265	-8.286	-3.224
p		.001	< .001	.002

Table 15. The ROC curve parameters of ALP, N-MID and TPINP

Markers	ALP	N-MID	TPINP
Area under the curve (95%CI)	0.695 (0.583–0.808)	0.734 (0.637–0.832)	0.837 (0.758–0.915)
p	.001	< .001	< .001
Cut-off value	120.72 U/L	19.00 mg/L	69.90 mg/L
Sensitivity (%)	56.80	54.10	67.60
Specificity (%)	82.90	87.10	85.70

SUV is a viable semi-quantitative parameter representing the tracer concentration corrected for body weight and injection activity. It is commonly used to assess the uptake of radionuclide tracers, reflecting the proliferation rate and metabolic activity of tumor tissue. It greatly aids in disease diagnosis, treatment efficacy evaluation and prognosis determination.[8, 12] Our study found that adenocarcinoma patients exhibited significantly lower SUVmax values in comparison to patients with squamous cell carcinoma and other types ($p < .05$); tumor diameter and TNM staging were independent factors influencing SUVmax. Patients with tumors > 5 cm in diameter and TNM stage III-IV demonstrated significantly higher SUVmax values in comparison to those with tumors $\leq$ 5 cm in diameter and TNM stage I-II ($p < .05$). Patients with tumors that are larger and at later stages may be more prone to bone metastasis. The higher SUVmax values observed in squamous cell carcinoma in comparison to adenocarcinoma may be attributed to the overexpression of glucose transporter-1 (GT-1) in squamous cell carcinoma cells, which results in a shorter doubling time and faster proliferation rate. Patients with tumors that are larger and at later stages exhibit relatively faster proliferation rates and higher metabolic activity, resulting in relatively higher SUVmax values.

Among various bone turnover markers, ALP is the most widely used marker of bone remodeling. Its advantage is that it is easier and less expensive to measure than other bone turnover markers. ALP is located in the osteoblast membrane and represents osteoblast activity.[13] Osteocalcin is a specific non-collagenous protein secreted by osteoblasts, with approximately one-third hydrolyzed into N-MID in peripheral blood. N-MID serves as a specific marker reflecting osteoblast activity, bone formation, and bone remodeling. TPINP is a specific type I collagen deposition marker that serves as an indicator of bone formation, with its levels significantly elevated during the occurrence of bone metabolic diseases. Our study found that ALP, N-MID and TPINP levels were significantly higher in patients with TNM stage III-IV in comparison to those with TNM stage I-II ($p < .05$). The areas under the ROC curves for ALP, N-MID and TPINP in diagnosing bone metastasis were all greater than 0.05, with TPINP (0.837) showing the highest value ($p < .05$). It indicates that patients in advanced stages are more prone to bone metastasis. ALP, N-MID and TPINP may serve as important biomarkers for distinguishing tumor staging and diagnosing bone metastasis, with TPINP demonstrating higher diagnostic value for bone metastasis. In advanced patients, tumor proliferation is rapid, making bone metastasis more likely to occur. Due to tumor invasion, osteoblast activity and metabolism become abnormal, leading to the elevated levels of ALP, N-MID and TPINP.

5. Conclusions

Serum levels of ALP, N-MID and TPINP are significantly elevated in patients with lung cancer bone metastasis in comparison to those without bone metastasis, while SUVmax shows no significant difference. SUVmax, ALP, N-MID and TPINP are associated with certain clinical and pathological characteristics in lung cancer patients. Among these, ALP, N-MID and TPINP demonstrate potential diagnostic value for lung cancer bone metastasis.

Acknowledgements

Not applicable.

Authors contributions

Hong Gu contributed to the study design and argumentation, literature search, data acquisition and organization, manuscript drafting; Guowei Tan and Qinghe Yu contributed to the data measurement on the subjects, data statistics and summary.

Funding

The study was funded by the Health and Hygiene Research Project of the Metallurgical Safety and Health Branch of the China Metallurgical Society (No. jkws202368).

Conflicts of Interest Disclosure

The authors declare no conflicts of interest.

Informed consent

Obtained.

ETHICS APPROVAL

The journal's policies adhere to the Core Practices established by the Committee on Publication Ethics (COPE).

PROVENANCE AND PEER REVIEW

Not commissioned; externally double-blind peer reviewed.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

DATA SHARING STATEMENT

No additional data are available.

OPEN ACCESS

COPYRIGHTS

REFERENCES

[1] Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. CA Cancer J Clin. 2022; 72(1): 7-33. PMid:35020204. https://doi.org/10.3322/caac.21708

[2] Tang M, Yang Y, Li G. Research Progress on Predictive Indicators and Models for Lung Cancer Bone Metastasis. Modern Medicine Journal of China. 2021; 23(11): 105-108.

[3] Ettinger DS, Wood DE, Aisner DL, et al. Non-Small Cell Lung Cancer, Version 3.2022, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2022; 20(5): 497-530. PMid:35545176. https://doi.org/10.6004/jnccn.2022.0025

[4] Ma Z, Wu Y, Wei W, et al. Predictive Model for the Risk of Bone-Related Events in Patients with Non-Small Cell Lung Cancer Bone Metastases. Guiding Journal of Traditional Chinese Medicine and Pharmacy. 2022; 28(7): 106-110.

[5] Hong F, Hu R, Xue T. Research Progress on the Mechanisms of Lung Cancer Bone Metastasis. Journal of Southeast University (Medical Science Edition). 2021; 40(5): 714-720.

[6] Zheng Q, Su J, Li X, et al. Differential Diagnostic Value of 18F-FDG PET/CT Imaging in Multiple Myeloma and Bone Metastases. Journal of Experimental Hematology. 2020; 28(4): 1267-1271.

[7] Lu J, Liu Y. New Advances in the Treatment of Lung Cancer Bone Metastases. Electronical Journal of Clinical Literature. 2019; 6(87): 197-198.

[8] Motegi K, Matsutomo N, Yamamoto T, et al. Evaluation of bone metastasis burden as an imaging biomarker by quantitative single-photon emission computed tomography/computed tomography for assessing prostate cancer with bone metastasis: a phantom and clinical study. Radiol Phys Technol. 2020; 13(3): 219-229. PMid:32535819. https://doi.org/10.1007/s12194-020-00571-6

[9] Wang S, Niu X, Bao X, et al. The PI3K inhibitor buparlisib suppresses osteoclast formation and tumour cell growth in bone metastasis of lung cancer, as evidenced by multimodality molecular imaging. Oncol Rep. 2019; 41(5): 2636-2646. PMid:30896825. https://doi.org/10.3892/or.2019.7080

[10] Chen Z, Chen X, Wang R. Application of SPECT and PET/CT with computer-aided diagnosis in bone metastasis of prostate cancer: a review. Cancer Imaging. 2022; 22(1): 18. PMid:35428360. https://doi.org/10.1186/s40644-022-00456-4

[11] Kitajima K, Tsuchitani T, Takahashi Y, et al. Usefulness of Quantitative Bone Single-Photon Emission Computed Tomography/Computed Tomography for Evaluating the Treatment Response of Bone Metastasis in a Lung Cancer Patient. Case Rep Oncol. 2021; 14(1): 391-396. PMid:33776734. https://doi.org/10.1159/000513907

[12] Yamane T, Fukushima K, Shirotake S, et al. Test-retest repeatability of quantitative bone SPECT/CT. Ann Nucl Med. 2021; 35(3): 338-346. PMid:33400148. https://doi.org/10.1007/s12149-020-01568-2

[13] Ebrahim T, Hadebe B, Aldous C, et al. Segmented linear correlations between bone scan index and prostate cancer biomarkers, alkaline phosphatase, and prostate specific antigen in patients with a Gleason score $\geq$ 7. Medicine (Baltimore). 2022; 101(25): e29515. PMid:35758394. https://doi.org/10.1097/MD.0000000000029515