Diagnostic efficacy of PET/CT in bone tumors

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Abstract. Clinical value of PET/CT (positron emission tomography/computed tomography) in the diagnosis of malignant bone tumors (BT) was investigated. Fifty-four patients with BT were first diagnosed by ordinary CT and then by PET/CT. The diagnostic efficacy outcomes and diagnosis of malignant BT by clinical stage of the two methods for BT were observed and recorded, and the diagnostic value of PET/CT in the diagnosis of BT was evaluated. There were 14 cases of benign BT patients, 15 cases of stage I, 10 cases of stage II and 15 cases of stage III in malignant BT patients. The diagnostic coincidence rate of PET/CT was 92.59% and the diagnostic coincidence rate of CT was 72.22%, which showed that the diagnostic coincidence rate of PET/CT was significantly higher than that of CT ($P<0.05$). The sensitivity, negative predictive value and positive predictive value of PET/CT were 95.00, 85.71 and 95.00%, respectively, which were higher than those of CT ($P<0.05$). CT and PET/CT were used for the clinical staging and pathological diagnosis of malignant BT; the results showed that the diagnostic accuracy of PET/CT in the clinical stages of malignant BT was also significantly higher than that of CT ($P<0.05$). The diagnostic efficacy of PET/CT in BT is better than that in CT. PET/CT can diagnose the pathological properties of BT more accurately, and can also effectively diagnose the clinical stage of malignant BT and provide clinical diagnostic basis for follow-up procedures.

Introduction

Bone tumor (BT) (1) is a tumor that occurs in the bone or its subsidiary tissues. BT are classified as benign BT and malignant BT. Benign BT is easy to cure and has a good prognosis, while malignant BT develops rapidly with poor prognosis and high mortality. The incidence of BT in the world (2) is low; but the absence of obvious symptoms or the neglect of minor symptoms in the early stage leads to misdiagnosis and missed diagnosis. Sometimes, it even develops into malignant BT at the time of a visit. PET/CT examination (3) is a common imaging detection method for the diagnosis of tumor. It is widely used in the differential diagnosis of various diseases. The diagnosis of BT has become a difficult problem in clinic because of its diverse causes and complex components. The clinical value of PET/CT in differential diagnosis of bone tumors and tumor-like lesions has also become a hot research topic (4).

PET/CT, a scanner combined by positron emission tomography and X-ray computed tomography, combines the two imaging techniques perfectly to form a complementary advantage (5). PET (positron emission tomography) provides functional and metabolic information (6) and CT (computed tomography) (7) provides detailed anatomical and pathological information. The pathophysiological and morphological changes of the disease can be obtained by the fusion of these two techniques. PET/CT is an advanced examination method. Its application in the diagnosis of tumors, especially BT, and the clinical value of differential diagnosis cannot be ignored. In addition, it is also non-invasive (8). Because of the existence of false positive and false negative, the result should be judged synthetically. In this study, CT was used as a control to evaluate the diagnostic efficacy of PET/CT in different stages of bone tumors.

Patients and methods

Clinical information. Fifty-four patients, including 34 males and 20 females with an age range of 15-75 years, with bone tumors (BT) treated in Henan Province Luoyang Orthopedic Traumatological Hospital (Henan Provincal Orthopedic Hospital) (Luoyang, China) from August, 2016 to February, 2018 were selected into this study. There were 14 cases of benign BT patients, 15 cases of stage I, 10 cases of stage II and 15 cases of stage III in malignant BT patients with clinical diagnosis (Table I).

Inclusion and exclusion criteria for the study were: i) Only BT patients admitted to Henan Province Luoyang Orthopedic Traumatological Hospital (Henan Provincal Orthopedic Hospital), lesions examined by pathology department and patients diagnosed as malignant BT and benign

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Key words: PET/CT, CT, bone tumors, diagnostic efficacy, tumor stage

Table I. Clinical information of BT patients.

Factors	n=54 [n (%)]
Age (years)	
≤36	21 (38.89)
>36	33 (61.11)
Sex	
Male	34 (62.96)
Female	20 (37.04)
Weight index (kg)	
Male (65.21±6.48)	34 (62.96)
Female (45.18±5.36)	20 (37.04)
Glycemic indices (mmol/l)	
<7.8	54 (100.00)
Lesion location	
Thigh-bone	8 (14.81)
Humerus	5 (9.26)
Shin bone	9 (16.67)
Radius	10 (18.52)
Ulna	5 (9.26)
Spine	8 (14.81)
Pelvis	9 (16.67)
Pathogenic condition	
Benign	14 (25.93)
Malignant	40 (74.07)
Lymphatic metastasis	
Yes	35 (64.81)
No	19 (35.19)

BT, bone tumor.

Table II. Manifestations of BT in PET/CT.

Variables	Manifestations in PET/CT
Benign BT	Bone tissue grew slowly, with no apparent or slight symptoms, clear periosteal edges, no periosteal reaction and no bone scan radioactive concentration.
Malignant BT	Periosteal edges were unclear. The soft tissue mass was obviously enhanced and the edge of the mass was clear. There were even cortical destruction, pathological fractures, bone lesions or bone scan radioactive concentration.

BT, bone tumor; PET/CT, positron emission tomography/computed tomography.

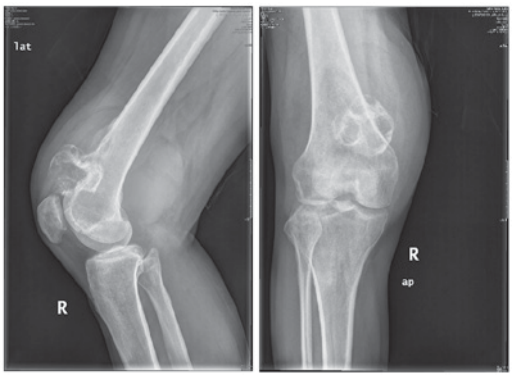

Figure 1. Malignant BT. In the anterior part of the right femur, a large mass-like abnormal density was observed. The density of the mass was uneven, and some of them were located in the suprapatellar capsule area. The cortical bone of the lower femur was destroyed, and the pericarp-like periosteal reaction was observed. The soft tissue of the patellar bursa and the lower end of the femur was significantly swollen, and the right knee was in place.

BT were included. ii) Pregnant women and patients with allergic reactions to contrast agents, claustrophobia and other contraindications were excluded. Informed consent was signed in advance by patients and their families. The present study was approved by the Ethics Committee of Henan Province Luoyang Orthopedic Traumatological Hospital (Henan Provincal Orthopedic Hospital).

Main reagents and instruments. PET/CT imaging agent: ^{18}F-deoxyglucose (^{18}FDG) was purchased from ACCDON Inc. (Waltham, MA, USA). PET/CT scanner was purchased from Royal Philips Electronics Co., Ltd. (Eindhoven, The Netherlands) and 64-slice spiral CT was purchased from Siemens AG (Munich, Germany).

Methods

PET/CT examination. Patients were weighed. The injection measurement of image agent should be controlled according to the patient's weight. Patients with BT should fast for at least 6 h before the examination. After 6 h, the venous blood glucose concentration of BT patients was measured to ensure that the blood glucose concentration was <7.8 mmol/l. The hospital needs to handle it in time when blood glucose concentration is too high or too low. ^{18}F-FDG imaging agent was injected into the patient's elbow vein after the patient's blood glucose concentration was within the normal range (the radiochemical purity should be >95%). Patients needed to empty their urine first and then drink 600 ml purified water before PET/CT examination. CT scan-fluoroscopic guidance was performed on the lesions of BT patients first; the PET was used to scan the largest range of BT lesions next, then the decay data of CT was corrected. The fusion images of CT, PET and PET/CT in all directions were then formed.

CT examination. All subjects were examined with 64-slice spiral CT with a slice thickness of 5-10 mm, a matrix of 512 x 512 mm. The soft tissue window and bone window parameters were set to 1,500-3,000 HU in window width and 300-700 HU in window level.

Judgement criterion. The diagnostic criteria for BT are as follows: i) The history of BT patients is completely clear. ii) PCT/CT showed that the concentration of bone nuclide was abnormal, the distribution was irregular and the distribution

Table III. Manifestations of BT in CT.

Variables	Manifestations in CT
Benign BT	The edges between BT lesion and periosteum was clear. Tumor invasion could be seen in bone marrow, but there were still normal bone marrow tissues.
Malignant BT	The edges between BT lesion and periosteum was unclear. There were changes in the adjacent tissue and swells or lumps in soft tissue; bone marrow was damaged and periosteal reaction occurred. Proliferation of tumor cells in bone marrow made it difficult to see normal bone marrow tissues. Tumor bone was produced.

BT, bone tumor; CT, computed tomography.

Table IV. Comparison between CT scan results and pathological diagnosis results.

Variables	Malignant BT diagnosed by pathology	Benign BT diagnosed by pathology	Total
Malignant BT diagnosed by CT	30	5	35
Benign BT diagnosed by CT	10	9	19
Total	40	14	54

BT, bone tumor; CT, computed tomography.

Table V. Comparison between PET/CT scan results and pathological diagnosis results.

Variables	Malignant BT diagnosed by pathology	Benign BT diagnosed by pathology	Total
Malignant BT diagnosed by PET/CT	38	2	40
Benign BT diagnosed by PET/CT	2	12	14
Total	40	14	54

BT, bone tumor; PET/CT, positron emission tomography/computed tomography

range was enlarged with time. Manifestations of BT in PET/CT are shown in Table II and Fig. 1. iii) CT or X-ray showed osteogenic destruction or osteolytic lesions in some bone tissues. Manifestations of BT in CT are shown in Table III. A patient who meets the first or last two criteria can be diagnosed as a BT patient. All images were evaluated by two or more relevant chief physicians.

Statistical methods. SPSS 17.0 (Beijing Bizinsight Information Technology Co., Ltd., Beijing, China) software system was used for statistical analysis; The enumeration data were represented by [n (%)]. An χ^2 test was used for a comparison of diagnostic accuracy of BT in different phases. Students' t-test was used for diagnostic accordance rate of CT and PET/CT. The difference was statistically significant at $P<0.05$.

Results

Analysis of diagnostic results. i) Comparison between PET/CT, CT scan results and pathological diagnosis results: 30 cases of malignant BT were detected by CT, and the positive predictive value was 85.71%, while 38 cases of malignant BT were detected by PET/CT, and the positive predictive value was 95.00%. Because CT scan was insensitive to the diagnosis of BT, the tissue imaging of adjacent disc was not clear; it was easy to cause misdiagnosis and missed diagnosis. Eight patients were screened as benign BT by CT, then screened as malignant BT by PET/CT, and confirmed as malignant BT by pathology at the same time (Tables IV and V); ii) Comparison of the diagnostic efficacy between PET/CT and CT in BT: The sensitivity, specificity, diagnostic accordance rate, negative predictive value and positive predictive value of CT screening were 75.00, 64.29, 72.22, 47.37 and 85.71%, respectively. While the sensitivity, specificity, diagnostic accordance rate, negative predictive value and positive predictive value of PET/CT screening were 95.00, 85.71, 92.59, 85.71 and 95.00%, respectively. There were significant differences in sensitivity, negative predictive value, positive predictive value and diagnostic accordance rate between PET/CT and CT screening ($P<0.05$). There was no significant difference in specificity between the two groups ($P>0.05$) (Table VI).

Comparison of the diagnostic efficacy between CT and PET/CT in different stages of BT. i) The diagnostic accordance rates of CT in benign BT and malignant BT were 64.29 and 75.00%, respectively. The diagnostic accordance rates of PET/CT in benign BT and malignant BT were 85.71 and 95.00%, respectively. The result showed that the diagnostic accordance rates of PET/CT in benign BT and malignant BT were higher than those of CT. The diagnostic rate of PET/CT in malignant BT was significantly higher than that of CT ($P<0.05$), and the difference was statistically significant (Table VII); ii) In comparison of the positive diagnostic rate between CT and PET/CT in different stages of malignant BT, the positive diagnostic rates of CT in stages I-III of malignant BT were 46.67, 90.00 and 93.33%, respectively. The positive diagnostic rates of PET/CT in the same stages were 86.67, 100.00 and 10.00%, respectively. Comparing the data of the two groups, it was found that the positive diagnostic rate of PET/CT in stages I-III of malignant BT was higher than that of CT, and the difference in stage I of malignant BT was statistically significant ($P<0.05$) (Table VIII).

Table VI. Comparison of the diagnostic efficacy between CT and PET/CT in BT.

Variables	CT [n (%)]	PET/CT [n (%)]	χ^2	P-value
Diagnostic accordance rate	39 (72.22)	50 (92.59)[a]	7.728	0.005
Sensitivity	30 (75.00)	38 (95.00)[a]	6.275	0.012
Specificity	9 (64.29)	12 (85.71)[b]	1.714	0.190
Negative predictive value	9 (47.37)	12 (85.71)[a]	5.122	0.024
Positive predictive value	30 (85.71)	38 (95.00)[a]	6.275	0.012

PET/CT, positron emission tomography/computed tomography; BT, bone tumor. [a]P<0.05 and [b]P>0.05, compared to CT.

Table VII. Diagnostic accordance rate of CT and PET/CT in benign BT and malignant BT (%).

Groups	CT	PET/CT	t	P-value
Benign group	64.29	85.71[b]	1.714	0.190
Malignant group	75.00	95.00[a]	6.275	0.012

PET/CT, positron emission tomography/computed tomography; BT, bone tumor. [a]P<0.05 and [b]P>0.05, compared to CT.

Table VIII. Comparison of the positive diagnostic rate between CT and PET/CT in different stages of malignant BT.

Stage	CT	PET/CT	χ^2	P-value
Stage I (n=15)	7 (46.67)	13 (86.67)[a]	5.400	0.020
Stage II (n=10)	9 (90.00)	10 (100.00)[b]	1.053	0.305
Stage III (n=15)	14 (93.33)	15 (100.00)[b]	1.034	0.309

PET/CT, positron emission tomography/computed tomography; BT, bone tumor. [a]P<0.05 and [b]P>0.05, compared to CT.

Discussion

The location of bone tumor (BT) is often in bone tissue or bone subsidiary tissue. Since BT in different stages has similar clinical and imaging manifestations, it is more difficult to diagnose BT in clinic. Relevant BT pathology (9) result shows that the clinical manifestations of partial benign BT are in a malignant state, and the effect of some benign BT-like lesions under X-ray (10) is particularly like that of malignant BT, and thus makes it more difficult to diagnose BT and BT-like lesions (11). At present, X-ray examination and CT scan are often used for early diagnosis or tumor staging of BT. Clinical application data (12) show that although X-ray examination can clearly reflect the location and size of BT in the BT staging diagnosis, it cannot accurately diagnose whether the BT is benign or malignant. Thus, the limitation of X-ray in the specific staging diagnosis of malignant BT is more obvious. CT can better display the fine anatomical structure of the location of BT when compared with X-ray examination. However, for improving the early diagnosis rate and the specific stage of BT patients, CT still lacks more precise function, metabolism and other molecular information (13) to assist BT staging diagnosis. PET/CT technology, which can integrate body function, metabolism and other molecular information, and accurate anatomical and pathological information, has been put into clinical application in recent years. A study (14) has confirmed that PET/CT is particularly sensitive for benign tumor, malignant tumor and early diagnosis of tumors.

The diagnostic efficacy of PET/CT and CT in BT was measured, and the results were compared and analyzed in the present study. It was found that the positive predictive value of CT in BT patients was 85.71%, while the detection rate of PET/CT in BT patients was 95.00%. In comparison, the detection rate of PET/CT in BT was significantly higher than that of CT. CT examination results of Janssen *et al* (15) found that CT imaging of adjacent disc tissue (16,17) was not very clear, and it was easy to cause misdiagnosis and missed diagnosis. While the results of different diagnostic efficacy of PET/CT and CT in BT showed that the sensitivity, specificity, diagnostic accordance rate, negative predictive value and positive predictive value of CT screening for BT were 75.00, 64.29, 72.22, 47.37 and 85.71%, respectively. While the sensitivity, specificity, diagnostic accordance rate, negative predictive value and positive predictive value of PET/CT screening were 95.00, 85.71, 92.59, 85.71 and 95.00% respectively. There were significant differences in sensitivity, negative predictive value, positive predictive value and diagnostic accordance rate between PET/CT and CT screening (P<0.05). There was no significant difference in specificity between the two groups (P>0.05). The diagnostic efficacy of PET/CT in BT is better than that of CT. The results of Guimaraes *et al* (18) were consistent with ours. They also applied the PET/CT technique to the comparative study of the diagnostic efficacy in BT, and compared it with other scanning techniques. By analyzing the scanning results of BT patients, they found that the sensitivity, specificity, diagnostic accordance rate, negative predictive value and positive predictive value of PET/CT were significantly higher than those of other scanning techniques, which was a good complement to our findings. Finally, the diagnostic efficacy of PET/CT in different stages of BT was analyzed concretely. The result showed that the diagnostic accordance rates of PET/CT in benign BT and malignant BT were higher than those of CT. The diagnostic rate of PET/CT in malignant BT was significantly higher than that of CT (P<0.05), and the

difference was statistically significant. Particularly in the stages I-III of the malignant BT, it was found that the positive diagnostic rate of PET/CT in stages I-III of malignant BT was higher than that of CT, and the difference in stage I was statistically significant ($P<0.05$). The accurate diagnostic efficacy of PET/CT in BT staging (19) has been confirmed in the clinical study of BT. The advantages of PET/CT in the diagnosis of BT or other tumors were summarized by El-Galaly *et al* (20), through extensive clinical data induction and comparison with other detection methods (21,22). They considered that the advantages of PET/CT in the diagnosis of different stages of tumor were that it could locate the lesion more accurately, detect the smaller lesion, and distinguish the benign, malignant and different stages of BT, abdominal neuroendocrine tumor and ovarian cancer, hepatocellular carcinoma by PET/CT imaging.

In this study, the selection of research objects was strictly in accordance with the inclusion and exclusion criteria to ensure the reliability of the results. However, due to the small number of subjects included, there were still some missed diagnosis and misdiagnosis for PET/CT in the detection of the diagnostic efficacy of PET/CT.

In conclusion, the diagnostic efficacy of PET/CT scan screening in different stages of BT is significantly better than that of CT. When CT scan screening is not accurate enough to judge BT staging, PET/CT can provide more precise tissue physiological metabolism and imaging evidence of anatomical structure of BT lesion. That is, PET/CT can accurately diagnose the pathological nature of BT, effectively diagnose the clinical stage of malignant BT, and provide more accurate clinical diagnosis basis for BT treatment.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

SH collected and interpreted the data, and wrote the manuscript. SH and YaL were mainly involved in PET/CT examination. YuL and MZ helped with the statistical analysis. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Henan Province Luoyang Orthopedic Traumatological Hospital (Henan Provincal Orthopedic Hospital) (Luoyang, China). Signed informed consents were obtained from the patients and/or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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