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Original Article

Correlation between imagenological and histological diagnosis of bone tumors. A retrospective study

Correlación entre el diagnóstico imagenológico e histológico de tumores óseos. Un estudio retrospectivo

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ABSTRACT. Introduction: The objective of this study was to retrospectively compare imaging techniques with histopathological findings from bone biopsy. **Material and methods:** Imaging techniques such as X-Ray, CT scan and MRI where compared with the histopathological findings from bone biopsy, in a population of 64 patients with bone tumors, with 64.1% of males and an age range of 5 to 79 years. **Results:** Histologically, 39.1% were malignant bone tumors, while 60.9% were benign. The X-ray showed 90% of diagnostic accuracy, with sensitivity of 92.9%, specificity of 87.5%, positive predictive value of 86.7% and negative predictive value of 93.3%. CT scan presented 75.9% of diagnostic accuracy, with 84.6, 68.8, and 84.6% of sensitivity, specificity, positive predictive value and negative predictive value, respectively. The MRI documented a diagnostic accuracy of 95.1%, with 94.4% os sensitivity, 95.7% of specificity, 94.4% of positive predictive value and 95.7% for negative predictive value. This showed a great agreement between the histology findings and those within the X-Ray and MRI (K = 0.8 and 0.9, respectively), but doesn't depreciate the value of bone biopsy in diagnosis of bone tumors. **Conclusion:** This data showed good correlation between imagenological and histopatologic techniques.

Keywords: Bone tumors, diagnostic, imaging, results, specificity.

RESUMEN. Introducción: El objetivo de este estudio fue comparar retrospectivamente las técnicas de imagen con los hallazgos histopatológicos de la biopsia ósea. **Material y métodos:** Las técnicas de diagnóstico por imágenes como rayos X, tomografía computarizada y resonancia magnética fueron comparadas con los hallazgos histopatológicos de la biopsia ósea, en una población de 64 pacientes con tumores óseos, con 64.1% de los varones y un rango de edad de cinco a 79 años. **Resultados:** Histológicamente, 39.1% eran tumores óseos malignos, mientras que 60.9% eran benignos. Los rayos X mostraron un 90% de precisión diagnóstica, con una sensibilidad de 92.9%, especificidad de 87.5%, valor predictivo positivo de 86.7% y un valor predictivo negativo de 93.3%. La tomografía computarizada presentó 75.9% de la precisión diagnóstica, con 84.6, 68.8, y 84.6% de sensibilidad, especificidad, valor predictivo positivo y valor predictivo negativo, respectivamente. La resonancia magnética documentó una precisión diagnóstica de 95.1%, con 94.4% de sensibilidad, 95.7% de especificidad, 94.4% de valor predictivo positivo y 95.7% para valor predictivo negativo. Esto mostró un gran acuerdo entre los hallazgos de histología y los que están dentro de la radiografía y la RMN (K=0.8 y 0.9, respectivamente), pero no deprecia el valor de la biopsia ósea en el diagnóstico de tumores óseos. **Conclusiones:** Estos datos mostraron una buena correlación entre técnicas imagenológicas e histopatológicas.

Palabras clave: Tumores óseos, diagnóstico, imagenología, resultados, especificidad.

Level of evidence: III.

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Introduction

Bone tumors are tissue masses formed by the abnormal growth of bone-like tissue. They can be classified as benign or malignant, primary or secondary (metastatic).[1] It's difficult to know the true incidence of each bone tumor, because many lesions are incidentally found on imaging exams and histologic diagnosis is not always requested, mostly in the presence of benign bone tumors.[2,3] Primary malignant bone tumors are relatively uncommon, they represent about 0.2% of all neoplasms in the human;[4] however they are an important cause of morbidity and mortality by cancer in children and adolescents.[1,2]

The diagnostic approach to focal bone lesions usually implies: clinical information (such as age, gender and personal history of malignancy); lesion localization; and radiographic benign/malignant appearance, regarding evaluation of margins appearance, cortical expansion grade, periosteal reaction and bone mineralization.[5,6,7,8] Additionally, CT and MRI can be used to a better characterization of the bone matrix, detection of mineralization, differential diagnosis and to determine the extension of the lesion.[5,6,9] Bone scintigraphy is useful to detect biological activity of the bone and evaluate the multiplicity of the lesions. PET shows the local metabolic activity of the tissue, but it is not yet globally available.[8] However, this information isn't always enough to classify a bone tumor.[1,8] Bone biopsy – image-guided needle aspiration or open incisional biopsy - is never the first diagnostic approach and its't performed in every patient; however it's considered the gold standard in the diagnosis of bone tumors.[1,5,8,10]

In the presence of a focal bone lesion, it's vital to be sure that malignant bone tumors aren't improperly omitted or that bone lesions aren't over treated, in order to provide the best possible management and outcome to the patient. Histology and imaging (especially radiographic appearance) have played a crucial role in the diagnosis of many benign and malignant bony lesions, but individually they carry some flaws in the definitive diagnosis of bone tumors. So we intended to establish the diagnostic agreement between imaging (X-Ray, CT and MRI) and histology in the diagnosis of bone tumors, taking open incisional bone biopsy as the gold-standard.

Materials and methods

Patient information from a Orthopaedic Reference Center, from 2004 to 2014, was retrospectively evaluated. The patients' selection was based on previous open incisional bone biopsy at this center, with confirmed histological diagnosis of bone tumor, benign or malign. This research retrieved 87 patients. The clinical files of all patients was analyzed, and patients who had available information on at least one more additional complementary diagnostic examination, being X-Ray, CT or MRI, were included. This information wasn't available for 23 patients, so we included 64 patients in the study. Age, gender and results from imaging, bone scintigraphy and histological examinations were recorded for each patient and analyzed using SPSS (Statistical Package for Social Sciences) 21.0 for Windows-Cohen's Kappa test for diagnostic correlation between each imaging technique and histopathology was obtained.

Table 1: Frequency of bone tumors.

Histology	Num. of cases	% Total	% In group
Malignant bone tumors	**25**	**39.1**	
Primary	**14**	**21.9**	
Ewing's sarcoma	6	0.9	
Plasmocytoma	5	0.8	
Osteosarcoma	3	0.5	
Secundary	**11**	**17.2**	
Benign bone tumors	**39**	**60.9**	
Cartilaginous tumors	**21**	**32.8**	53.8
Osteochondroma	13	20.3	
Enchondroma	7	10.9	
Chondromyxoid fibroma	1	0.1	
Osteogenic tumors	**5**	**0.8**	12.8
Osteoid osteoma	3	0.5	
Osteoblastoma	2	0.3	
Vascular tumors	**3**	**0.5**	0.8
Hemangioma	3	0.5	
Lipogenic tumors	**1**	**0.1**	0.3
Lipoma	1	0.1	
Fibrogenic tumors	**1**	**0.1**	0.3
Desmoplastic fibroma	1	0.1	
Miscellaneous tumors	**7**	**1.1**	17.9
Aneurysmal bone cyst	4	0.6	
Histiocytosis X	1	0.1	
Simple cyst	1	0.1	
Non ossifying fibroma	1	0.1	

Results

From the 64 patients included in the study, 64.1% (41) were male, with 35.9% (23) females. The age ranged from 5 to 79 years, with mean age of 33.5 ± 27 and median age of 27 years, with 50% of the sample younger than 25 years and peak incidence from 11 to 20 years and above 50 years.

Histologically, 25 (39.1%) were malignant bone tumors, whereas 39 (60.9%) were benign bone tumors. In the malignant tumors group, 14 were primary bone tumors (6 Ewing's sarcoma, 5 plasmocytomas and 3 osteosarcoma), while 11 were Secondary bone tumors. Considering the benign bone tumors, the most common type was cartilaginous bone tumor (21 cases-53.8%), with 13 osteochondromas. The frequency of bone tumors is showed in *Table 1*.

Tables 2 and 3 document the comparison of histological diagnosis with X-Ray of bone tumors. Of the 30 patients who were submitted to an X-Ray, only one malignant tumor had a wrong diagnosis of benign tumor and two benign tumors were

classified as malignant, with a diagnostic accuracy of 90%, and a Cohen's kappa value of 0.8 (> 0.75) *(Table 2 and 3)*.

Considering all patients, 29 (45.3%) were submitted to a CT scan for diagnostic evaluation, alone or in combination with others exams. The comparison of histological versus radiological bone tumors is showed in *Tables 4 and 5*. With this technique, the diagnostic accuracy was 75.9%, with a corresponding Cohen's kappa value of agreement of 0.522 *(Table 4 and 5)*.

In total, 41 patients (64.1%) were submitted to an MRI, subsequently to other complementary diagnostic means or not. The results obtained in the comparison of histological versus MRI diagnosis in these patients are displayed in *Tables 6 and 7*. In this case, the Cohen's kappa value for the correlation was 0.9, with a diagnostic accuracy of 95.1% *(Table 6 and 7)*.

Bone scintigraphy was performed additionally in 26 patients (40.6%). Comparison of this examination versus imagiological diagnosis (X-Ray, TC or MRI), showed agreement in 21 cases (80.8%), with 5 (19.2%) cases in which the technique suggested a different pathology.

Regarding the definitive classification of the bone tumor, according to the WHO classification of bone tumors,[3] the X-Ray diagnosed correctly 17 of 27 cases (63.0%), with misinterpretation of 2 cases of Ewing's sarcoma as osteosarcoma and the case of chondromyxoid fibroma as aneurysmal bone cyst.

TC succeeded to classify 17 of 22 patients (77.3%). Although, two cases of Ewing's sarcoma were interpreted as osteosarcoma, and two plasmocytomas were classified as metastatic malignancy.

Table 2: Comparison of histological versus X-Ray diagnosis of bone tumors.

Radiological diagnosis	Histological diagnosis (gold standard)		Total
	Malignant bone tumor	Benign bone tumor	
Malignant bone tumor	13 (TP)	2 (FP)	15
Benign bone tumor	1 (FN)	14 (TN)	16
Total	14	16	30

TP = true positive; FP = false positive; FN = false negative; TN = true negative.

Table 3: Sensitivity, specificity, diagnostic accuracy, PPV and NPV of diagnosis with X-Ray.

	%
Sensitivity	92.9
Specificity	87.5
Diagnostic accuracy	90.0
Positive predictive value	86.7
Negative predictive value	93.3

Table 4: Comparison of histological versus CT diagnosis of bone tumors.

TC diagnosis	Histological diagnosis (gold standard)		Total
	Malignant bone tumor	Benign bone tumor	
Malignant bone tumor	11 (TP)	5 (FP)	16
Benign bone tumor	2 (FN)	11 (TN)	13
Total	13	16	29

TP = true positive; FP = false positive; FN = false negative; TN = true negative.

Table 5: Sensitivity, specificity, diagnostic accuracy, PPV and NPV of TC diagnosis.

	%
Sensitivity	84.6
Specificity	68.8
Diagnostic accuracy	75.9
Positive predictive value	68.8
Negative predictive value	84.6

Discussion

This is, to our knowledge, the first comparative study of the spectrum and diagnostic accuracy of bone tumors from a reference center. Lack of information available in patient's clinical files limited the inclusion of a larger sample of patient's. This might be related to the time interval we analyzed, because information kept prior to digital recording is hard to obtain and less organized.

Our sample of 64 bone tumors, showed a predominance for the male gender, with 64.1% (41) males, which is comparable to the results of Settakorn et al.[11] and Naz et al.[12] of 54.9 and 66.7% of males, respectively; Negash et al,[1] obtained a male to female ratio of 1.08:1.

Age distribution was comparable to other studies. Like us, Negash et al.[1] and Naz et al.[12] recorded a peak incidence of bone tumors from 10 to 20 years. 50% of our patients had less than 25 years, whereas Negash et al.[1] had 77.1% of the patients below 30 years, and the Pakistan study[12] had 50% of patients with less than 20 years; Settakorn et al,[11] described 60% of the patients as being younger than 30 years. We documented a second peak of incidence, with 26.6% of patients in the group of more than 50 years, which didn't happen in other studies. Naz et al.[12] and Negash et al,[1] only included patients until 55 and 65 years, respectively, a fact that probably explains this difference.

The most common primary malignant tumor is the plasmocytoma, followed by osteosarcoma, chondrosarcoma, Ewing's sarcoma-those three with a much lower incidence.[3] Concerning primary benign tumors, the most common are the osteochondroma (35%) and the enchondroma (20%).[3]

Metastatic involvement of the musculoskeletal system is by far the most common bone tumors category – 50% of all malignancies diagnosed annually can metastasize to the bone. It's origin is preferentially from the prostate, breast, lung, thyroid and kidney.[3]

Despite our sample might look limited, we managed to corroborate some of these descriptions: our set of primary malignant bone tumors only revealed Ewing's sarcoma (0.9%), plasmocytomas (0.8%) and osteosarcoma (0.5%) and our most common benign tumors were cartilaginous (53.8% of all benign lesions), with prevalence of osteochondroma and enchondroma – 20.3 and 10.9% of all tumors, respectively. Metastatic malignancies only represented 17.2%[12] of all patients, and this might be related to a diminished need to perform a bone biopsy for the differential diagnosis in these cases, compared to those of suspected primary bone tumor. However, similar studies with larger samples revealed comparable findings: Settakorn et al.[11] and Negash et al.[1] reached, respectively, 10.4 and 5.5% of metastatic malignancies. This last study also reported a higher frequency of cartilaginous benign tumors, with 25.9% of the total, although with a very high detection of osteosarcoma, representing 21.9% of all the patients. On the other hand, the Thai study,[11] with 1,001 patients, showed an osteosarcoma frequency closer to ours (2.5%), with cartilaginous tumors as the most common group of benign tumors (29.7%). Despite this, they reported Giant Cell Tumors as the most common lesions (3.7%), comparable to what happened in the Naz et al study,[12] with 20%.

There aren't a lot of reports correlating imaging and histology in the diagnosis of bone tumors. Our results from comparison of radiological versus histology findings in bone tumors can be compared with the ones from Naz et al,[12] Lee et al[13] and Negash et al.[1] The Pakistan study documented sensitivity, specificity, diagnostic accuracy, PPV and NPV of 83.3, 100, 93.3, 100 and 93.3%, while we obtained 92.9, 87.5, 90, 86,7 e 93.3%, respectively. Lee et al[13] reported 80% sensitivity and a specificity of 93%, in assessing the radiographic appearance of bone tumors. The larger African study from Negash et al[1] obtained a lower diagnostic accuracy of 84%, with a Cohen's kappa value of 0.82, similarly to ours of 0.8.

To our knowledge, this is the first documentation of the correlation of CT and MRI with histology findings in the diagnosis of bone tumors. Comparison of CT versus histology findings revealed sensitivity, specificity, diagnostic accuracy, PPV and NPV, respectively, of 84.6, 68.8, 75.9, 68.8 and 84.6%, with a Cohen's kappa value 0.5; while the same analyzes for MRI documented sensitivity, specificity, diagnostic accuracy, PPV and NPV of 94.4, 95.7, 95.1, 94.4 and 95.7%, respectively, with a corresponding Cohen's kappa value of 0.9.

A Cohen's kappa statistic > 0.75 shows a great level of agreement between different raters, so we found that X-Ray (K = 0.8) and MRI (K = 0.9) have a good diagnostic capacity for bone tumors. CT showed a worse performance in this matter (K = 0.5).

Bone scintigraphy wasn't used as a single diagnostic approach in any patient, and revealed useful in corroborating the presence or absence of the pathology previous suggested by an imaging exam, since it agreed with other diagnostic techniques in 80.7% (21 out of 26) of the patients. So, it has proved to be a sensitive exam with special value in patients with a primary known tumor, to determine the presence and extension of metastatic disease.[2,8]

Regarding the diagnosis according to the WHO classification of bone tumors,[4] the X-Ray classified wrongly 2 cases of Ewing's sarcoma as osteosarcoma and the case of chondromyxoid fibroma as aneurysmal bone cyst; this results can be compared to those of Negash et al,[1] who reported 1 case of osteosarcoma with radiographic appearance of plasmocytoma, while in seven cases the X-Ray suggested osteosarcoma and the definitive histologic diagnosis was different. In our study, CT also interpreted two cases of Ewing's sarcoma as osteosarcoma, as well as 2 plasmocytomas as metastatic malignancy.

These findings might arise some justified concern. Despite the low frequency of bone sarcomas, these particularly affect children and adolescents; so, because of its impact on families it's important to manage these as correctly as possible.[2] Osteosarcoma is one of the most common primary bone tumors, which may justify somewhat the trend that has occurred in this study for the wrong classification as osteosarcoma by imaging exams in some patients. The evaluation of the site of the injury for each bone tumor could eventually help to understand if that factor misleads the diagnosis, since Osteosarcoma is more frequent around the knee.

Table 6: Comparison of histological versus MRI diagnosis of bone tumors.

MRI diagnosis	Histological diagnosis (gold standard)		Total
	Malignant bone tumor	Benign bone tumor	
Malignant bone tumor	17 (TP)	1 (FP)	18
Benign bone tumor	1 (FN)	22 (TN)	23
Total	18	23	41

TP = true positive; FP = false positive; FN = false negative; TN = true negative.

Table 7: Sensitivity, specificity, diagnostic accuracy, PPV and NPV of MRI diagnosis.

	%
Sensitivity	94.4
Specificity	95.7
Diagnostic accuracy	95.1
Positive predictive value	94.4
Negative predictive value	95.7

Also important is to focus that the wrong classification of a lesion as being a metastatic malignancy may have important consequences, namely: the fruitless search by doctors of a primary occult neoplasm, subjecting the patient to unnecessary exams; along with a delay in the beginning of treatment or even the application of a wrong treatment; and the important emotional burden to the patient. Bone biopsy can put an end to these problems and may prove to be an important approach whenever available, especially in younger patients with suspected primary bone lesions, in order to make the best use of the recent advances in treatment modalities.[2,8]

Thus, although most of the situations are correctly managed applying imaging exams and avoiding invasive procedures, it is crucial to balance the risks and benefits individually to each patient.

Existing publications on this matter, only concern the diagnostic capacity of imaging techniques applied together, without accessing the value of each one on its own. Since the diagnosis of a focal bone lesion isn't, in the majority of the times obtained with only one diagnostic exam, the acknowledgment of the validity of each technique by itself is also important to decide when to consider a certain finding correct or not in order to be able to better differentiate cases in which further examination, as bone biopsy, might be the correct approach.

Conclusion

This is, to our knowledge, the first study correlating histology findings with each imaging technique – X-Ray, CT and MRI – in the diagnosis of bone tumors. We reported a great agreement between the histology findings and those within the X-Ray and MRI (K=0.8 and 0.9, respectively), with worse results concerning diagnosis by CT (K = 0.5). This reinforces the use of imaging techniques to evaluate focal bone lesions; however, findings of wrong diagnosis may be taken in consideration by clinicians, and requisition of bone biopsy must be considered whenever available.

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