Comparison of the diagnostic value of low dose computed tomography of the axial skeleton and skeletal radiography in patients with multiple myeloma

Comparación del valor diagnóstico de la tomografía computarizada de dosis baja del esqueleto axial y la radiografía esquelética en pacientes con mieloma múltiple.

*Yaseen M. Taher FIBMS (HEMATO), CABMS, dr.yaseen1979@gmail.com Safa Hussam FIBMS, safa.hussam2011@gmail.com
Hussam Dawod Saeed FIBMS, abodi_bmw@yahoo.com
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Abstract

Background: Multiple myeloma (MM) is a plasma cell neoplasm characterized by bone marrow infiltration and clonal proliferation of plasma cells. The detection of lytic bone lesions represents a criterion defining a symptomatic and treatment-requiring MM. **Aim of the study:** To compare the accuracy of whole body low dose CT (WBLDCT) versus skeletal radiographs in detecting myeloma lesions and to establish the feasibility of (WBLDCT) protocol as an alternative to conventional X-ray imaging. **Patients and Methods**: A cross sectional analytical study had been conducted in Al- Yarmouk teaching hospital in Baghdad. A total of 41 patients, their ages range between 40 – 82 years, diagnosed with multiple myeloma, underwent WBLDCT and digital radiography (DR). **Results**: There was weak agreement between WBLDCT and X-ray in detection of lytic lesions in skull, spine and pelvic bones with (Kappa = 0.382, p = 0.007) for skull, (Kappa = 0.147, p=0.077) for spine, (Kappa = 0.223, p = 0.023) for pelvic bones. WBLDCT identified more osteolytic lesions than radiograph with total number of lesions detected with WBLDCT was 520 versus 152 for radiographs (p<0.001). **Conclusion:** Whole body Low-dose CT is superior to skeletal radiography with a comparable radiation dose for detection of lytic lesions of MM, with a fast scanning time and high resolution images.

Keywords: whole body low dose computed tomography (WBLDCT), lytic lesions, skeletal radiograph, multiple myeloma.

Resumen

Antecedentes: el mieloma múltiple (MM) es una neoplasia de células plasmáticas caracterizada por infiltración de la médula ósea y proliferación clonal de células plasmáticas. La detección de lesiones óseas líticas representa un criterio que define un MM sintomático y que requiere tratamiento. Objetivo del estudio: Comparar la precisión de la TC de baja dosis de cuerpo entero (WBLDCT) frente a las radiografías esqueléticas en la detección de lesiones de mieloma y establecer la viabilidad del protocolo (WBLDCT) como alternativa a las imágenes de rayos X convencionales. Pacientes y métodos: A Se realizó un estudio analítico transversal en el hospital universitario Al-Yarmouk en Bagdad. Un total de 41 pacientes, con edades entre 40 y 82 años, diagnosticados con mieloma múltiple, se sometieron a WBLDCT y radiografía digital (DR). Resultados: hubo concordancia débil entre WBLDCT y rayos X en la detección de lesiones líticas en cráneo, columna y huesos pélvicos con (Kappa = 0.382, p = 0.007) para cráneo, (Kappa = 0.147, p=0.077) para columna, (Kappa = 0,223, p = 0,023) para huesos pélvicos. WBLDCT identificó más lesiones osteolíticas que la radiografía con un número total de lesiones detectadas con WBLDCT de 520 frente a 152 para radiografías (p<0,001). Conclusión: la TC de dosis baja de cuerpo entero es superior a la radiografía esquelética con una dosis de radiación comparable para la detección de lesiones líticas de MM, con un tiempo de escaneo rápido e imágenes de alta resolución.

Palabras clave: tomografía computarizada de baja dosis de cuerpo entero (WBLDCT), lesiones líticas, radiografía esquelética, mieloma múltiple.

Multiple myeloma is a plasma cell neoplasm characterized by bone marrow infiltration and clonal proliferation of plasma cells which may produce excessive amounts of monoclonal immunoglobulin's that can be detected in serum and urine[1,2] Multiple myeloma and osteosarcoma combined account for approximately 50% of all primary bone malignancies. The osteolytic destruction of the bony skeleton in multiple myeloma distinguishes it from precursor entities such as monoclonal gammopathy of undetermined significance (MGUS) and smoldering myeloma[3]. The CRAB criteria proposed by the International Myeloma Working Group (IMWG) that define symptomatic multiple myeloma requiring therapy, include an imaging evaluation of the skeleton[3] because the detection of lytic bone lesions represents a criterion defining a symptomatic and treatment-requiring MM[4,5].

According to the Durie-Salmon-Staging system, the presence and number of osseous lesions contribute directly to the staging of the disease and thereby to the risk stratification of MM [6] (table 1)

The use of more sophisticated imaging techniques, such as computed tomography (CT) help to better define osteolytic lesions allowing for earlier detection of the disease. Whole body low-dose CT has replaced conventional radiography at many European centers [7,8].

Table 1. [6] Assessment of myeloma tumor mass (Salmon-Durie)

stage 1(low cell mass) **All of the following must be present**
A. Hemoglobin value > 10.5 g/dL B. Serum calcium value normal or <10.5 mg/dL C. Low M-component production rates: 1. IgG value < 5g/dL 2. IgA value < 3 g/dL 3. Urine light chain M-component < 4 g/24h D. No bone lesion or osteoporosis
Stage II((intermediate red cell mass) Fitting neither Stage I nor Stage III
All patients who do not qualify for high or low tumor mass categories are considered to have intermediate tumor mass
stage III (high tumor mass): One or more of the following
A. Hemoglobin value < 8.5 g/dL B. Serum calcium value > 12 mg/dL C. High M-component production rates 1. IgG value > 7 g/dL; 2. IgA value > 5 g/dL 3.Urine light chain M-component > 12 g/24h D. > 3 lytic bone lesion on bone survey

Aim of the study

To compare the accuracy of whole body low dose CT (WBLDCT) versus radiographs in detecting myeloma lesions and to establish the feasibility of (WBLDCT) protocol as an alternative to conventional X-ray imaging.

Patients and methods

A cross sectional analytical study included a total of 41 patients, diagnosed with multiple myeloma, their age range between 40 – 82 years from January 2017 to December 2017. WBLDCT protocol study performed on a 64-slices scanner, with tube voltage 120 kVp; tube current time product 40 mAs increase to 50 in obese patients. The scan length was stretched from the roof of the skull down to the proximal femur. Images were reconstructed in 1 mm sections using filter and hybrid iterative reconstruction technique (SAFIRE). Multi planar reformations were made in the sagittal, coronal and axial plane. Two radiologists assessed the presence and number of osteolytic lesions at three anatomical regions: skull, spine and pelvis and compared with X-ray images finding. The assessment of bone density was done on a subjective basis as well as objectively by measuring the bone density based on the Hounsfield units using simple trabecular ROI attenuation approach, value of less than 120 was indicates likely bone osteopenia.

Calculation of the radiation dose

The effective radiation dose from CR was estimated from literature data & tables for typical effective dose in diagnostic radiology for the 3 projections (lateral skull 0.04 mSv, lateral spine 1.1 mSv and AP pelvis 0.6 mSv)[9,10].

The radiation dose from WBLDCT was estimated using the dose length product (DLP) and k Coefficients from the European Guide lines.

Results

At this study Female to male ratio was 1.3:1, Mean age of the patients 58.88 ± 10.77 years ranging from 40 – 82 years, most of the patients were in the age groups 60 – 69 years, and 50 – 59 years. There was slight agreement between WBLDCT and X-ray in detection of lytic lesions in skull bones. In which from total 41 patients undergone skull X-ray, 19 patients (46.3%) show detection of lytic lesions. While the remaining 22 patients (53.6%) were negative.

Regarding the skull LDCT, from total 41 patients 28 patients (68.3%) show detection of lytic lesions. While the remaining 13 patients (31.7%) were negative

There was concordance in 17 cases diagnosed with lytic lesions between skull LDCT and skull X-ray, and concordance in 11 cases were negative in both skull LDCT and skull X-ray

Also There was weak agreement between WBLDCT and X-ray in detection of lytic lesions in spine &pelvic bones.

Total number of skull lesions detected by WBLDCT was 126, compared to 86 lesions detected by X-ray ($p < 0.001$) with detection rate 1.4. Total number of spine lesions detected by WBLDCT was 214, compared to 36 lesions detected by X-ray ($p < 0.001$) with detection rate 5.9. Total number of pelvic lesions detected by WBLDCT was 180, compared to 30 lesions detected by X-ray ($p < 0.001$) with detection rate 6. In total

WBLDCT has a higher detection rate of lytic lesions compared with X-ray with a detection rate about 3.4 fold higher (520 vs. 152), The differences between the two methods turned out to be most obvious at the spine and pelvis (six-fold).

In the WBLDCT The spine bone offers the highest number of lytic lesions followed by pelvic and skull; On X-ray the skull represents the best bone for determining the lytic lesions compared to both spine and pelvic (Table 2).

Table 2. Total number of lytic lesions in WBLDCT

	Skull	Spine	Pelvic
Total lesions	**126**	**214**	**180**
Mean	3.073	5.22	4.39
95%CI of mean	1.7 - 4.446	3.478 - 6.961	2.815 - 5.965

Estimation of radiation dose and examination time

The effective dose from lateral skull, lateral spine and from AP pelvis X-ray was estimated as 1.7 milliseverts (mSv) per patient. In comparison, the overall dose delivered to each patient from WBLDCT was 4.3 mSv for a tube current of 40 mAs and 5.2mSv for 50 mAs. With DLP values (289 & 348) for 40 mAs & 50 mAs respectively.

It should be also emphasized that WBLDCT was much faster, as compared to the set of radiographs that require special positioning for every projection. In-room time for CR was approximately 15 min. In-room time for MDCT was 5 min including patient registration and positioning as well as scanning (approximately 30 s).

Discussion

Radiography is still the main imaging tool in MM patients; However, MM lesions can be detected on plain films only when more than 30–50% of trabecular bone loss is evident. Thus, early myeloma may not reveal any detectable change on Conventional Radiology. Different studies demonstrated major limitations of such a radiological skeletal survey due to frequently false-negative findings[9-11]. Thus, imaging modalities alternative to the X-ray survey have been searched.

With the development of the multi detector technology, whole-body scanning using thin collimation protocols could be performed routinely, enabling the coverage of larger body regions with acceptable image quality. Low dose CT protocols with either 120 or 100 kV peak tube voltage and 40–100 mAs planned tube time-current have been used with or without iterative reconstruction technique, with a resulting radiation exposure between 4 and 10 mSv [8,12]. The radiation dose in our WBLDCT protocol was 4.3 mSv and this is comparable to and in agreement with the values obtained in Princewill et al[12] and kropil et al.[2].

In this study the estimated effective dose from X-ray was (1.7 mSv) and it was taken from reference tables of effective radiation dose this was in agreement with kropil et al.[2] (1.7mSv).

In this study , the difference in dose between x-ray and WBLDCT (1.7 mSv vs. 4.3 mSv respectively) is not of big issue as Many of MM patients are treated with radiotherapy that uses doses about a thousand times larger than the diagnostic doses in CT. Mean age of the patients in the present study was 58.88±10.77 years ranging from years, this was near to Kropil et al[2] (in which the median was 57 years (range: 44–73) and Princewill et al[12] (in which the median age was 56 years (range of 35–73 years). Female to male ratio in presenting study was 1.3:1 which was in disagreement with other studies in which male was more common than female (female to male ratio 1:1.2). Probably small sample in our study can explain this variation.

In the present study 5 out of 41 patients (12.1%) had no detectable findings on either X-ray or WBLDCT &the remaining 36patients(87.8%) had more lesions detected by WBLDCT than by CR including 8 patients (19.5%) showed osteolytic lesions in WBLDCT although CR was negative, while no patients had more lesions detected by X-ray than WBLDCT and this was near to results from Kropil et al[2] in which 4 out of 29 patients (13.7%) had no detectable findings on either X-ray or WBLDCT & 5 out of 29 patients (17.2%) had osteolytic lesions in WBLDCT where is CR was negative

Our results were slightly lower than that seen by Princewill et al.[12], in which 9 out of 51 patients (18%) had no detectable findings on either X-ray or WBLDCT, and the remaining 39 of 42 (93%) patients had more lesions on CT while 3 of 42 patients had more lesions detected on X-ray than WBLDCT. This may be related to the variation in patients demographic, sample numbers and also because x-ray interpretation may be affected by technical factors and the experience and training of the personnel taking the radiograph

In the present study, there was weak agreement between WBLDCT and X-ray in detection of lytic lesions in spine and pelvic bones, in which from 41 patients 23 patients (56%) &19 patients (46%) respectively show lytic lesions by WBLDCT but they were negative in CR taken for these regions, and that was approximate to results from Kropil et al[2] in which from 29 patients 15 patients (51%) &12 patients (41%) show lytic lesions by WBLDCT in spine and pelvis respectively but they were negative in CR taken for these regions.

In the present study we found a much higher detection rate of lytic bone lesions in WBLDCT in comparison to X-ray. From 41 patients the total number of lytic lesions detected by X-ray were 152, comparable to 520 lytic lesions detected by WBLDCT (ratio of detection 3.4) and this was approximately in agreement with Princewill et al.[12] in which in 51 patients including in their study, the total number of lytic l lesions detected by CR were 248, while by WBLDCT were 968 lytic lesions (ratio of detection was 3.9).

This study shows the detection rate concerning the spine and pelvic skeleton was significantly higher ($p \leq 0.001$), the spine and pelvis LDCT detect approximately 6 fold more lytic lesions than X-ray at these regions. This is easily attributable to overlapping osseous structures and soft tissues in these re-

gions, which obscure subtle (and sometimes obvious) lesions on routine radiographs, while the skull LDCT shows inferior detection rate in comparable with spine and pelvis, however it still has higher detection rate 1.4 than skull X-ray and this was in agreement with Princewill et al[12] which also shows significantly higher detection rate at the spine and pelvis 4.9 and 6.6 respectively (p≤0.001) and lesser at skull 1.09 **(Table 3)**. kropil et al[2] also shows significantly higher detection rate at the spine and pelvis 4.6 and 2.5 respectively (p≤0.001), however it is lower than our rate and this may be attributable to lower number of samples taken by them which was 29 patients.

In the present study WBLDCT shows that the spine was the most frequently involved bone in which from total 41 patients 78% shows lytic lesions in vertebral column with a total number of lytic lesions 214 lesion, this was in agreement with Princewill et al.[12] and kropil et al.[2] .

Considering that the X-ray examination causes patients discomfort in relation to the multiple postures required for overall bone examination, the reduction of acquisition time represents an important advantage[12-15]. The present study has some limitations. Firstly we cannot take a complete series of skeletal survey in our MM patients (it require along acquisition time and the patients cannot tolerate it) also the X-ray films taken only on one equipment Finally, the study group was non homogeneous, and most of the patients had previously undergone treatment.

Table 3. Detection rate of osteolytic bone lesion number by body region (WBLDCT vs. X-Ray)

	Princewill et al.[12]				Present study			
	WBLDCT (# detected)	X-ray (# detected)	Ratio of detection (WBLDCT#/X-ray#)	P	WBLDCT	X-ray (# detected)	Ratio of detection (WBLDCT#/X-ray #)	P
Total skeleton	968	248	3.9	<0.001	520	152	3.4	<0.001
Skull	94	86	1.09	0.02	126	86	1.4	
Spine	241	49	4.92	<0.001	214	36	5.9	<0.001
Pelvis	240	36	6.67	<0.001	180	30	6	<0.001

Conclusions

WBLDCT with a hybrid iterative reconstruction technique is superior to skeletal radiography with a comparable radiation dose for detection of lytic lesions of MM. It is a reliable and feasible imaging-based tool for evaluating patients with MM, particularly in regions that are superimposed in the skeletal radiographs. This is mainly because of its Short acquisition time, Easy reproducibility contrast -or preparation time necessary), High patient tolerance (patients in the supine position without needing repeated relocation).

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