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The role of opportunistic quantitative computed tomography in the evaluation of bone disease and risk of fracture in thalassemia major

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Abstract

Objective: Dual-energy X-ray absorptiometry (DXA) remains the cornerstone for osteoporosis evaluation in Thalassemia major. However, several drawbacks have been observed in this unique setting. We sought to determine the correlation between quantitative CT (QCT) and DXA-derived parameters; secondarily, we aimed to investigate the role of the two techniques in predicting the risk of fracture.

Methods: We retrospectively included patients with β-thalassemia major who had undergone both lumbar and femoral DXA examinations, and CT scans including the lumbar spine, performed for disparate diagnostic issues, within 4 months from the DXA. CT data were examined employing a phantom-less QCT method for bone mineral density (BMD) assessment. We also retrieved any spontaneous or fragility fractures occurring from 1 year before up to 5 years after the date of DXA scans.

Results: The 43 patients were included. QCT measures were significantly higher than those determined by DXA. The gap between QCT and DXA values was strongly associated with patient age. The most powerful predictive variable for risk of fracture was the ACR classification based on volumetric BMD obtained by QCT.

Conclusions: DXA provided more negative measures than those determined by QCT. However, QCT seemed to evaluate thalassaemic osteopathy better than DXA, since volumetric BMD was a stronger predictor of fracture.

KEYWORDS

thalassemia, dual-energy x-ray absorptiometry, x-ray computed tomography, osteoporosis, fractures

1 | INTRODUCTION

Osteoporosis constitutes a frequent and major complication in patients with thalassemia, and its prevalence is presumed to increase since life expectancy of affected patients has significantly improved due to optimized transfusion programmes associated to adequate iron chelation.[1]

Osteoporosis is generally defined by low bone mass and microarchitectural deterioration of bone tissue, leading to an increase in

bone fragility and the risk of fracture. The characteristics of thalassemia-associated osteoporosis are, however, unique compared to those of the more typical idiopathic osteoporosis observed in the general community as a result of several factors contributing to the complex pathophysiology and management of this condition.[2–5]

Measurement of areal bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) of the spine and hip represents the cornerstone for osteoporosis diagnosis and therapy monitoring.[6]

However, numerous drawbacks for the use of DXA have been observed in thalassaemic subjects, with several open issues related to their young age, the presence of bone deformities and degenerative changes, and the reduced skeletal size due to the failure to reach peak bone mass.[7]

Moreover, the role of DXA in assessing fracture risk is far less clear in this population as compared to postmenopausal patients. The risk of fracture is indeed a composite of multiple factors, many of which will cause substantial deterioration in bone microarchitecture without a concomitant decrease in areal BMD as measured by DXA.[3]

A relatively recent trend in osteoporosis imaging originates from the large amount of computed tomographic (CT) exams performed in clinical routine. In the past decades, we have witnessed a steady increase in the number of CT examinations obtained for diverse purposes, a large proportion of which presumably includes vertebrae. Using previously acquired CT data provides an interesting opportunity for osteoporosis screening. Several studies in recent years have exploited this possibility, but the actual role of opportunistic screening in official osteoporosis guidelines is still unclear.[8]

In this study, we primarily sought to determine the correlation of opportunistic quantitative CT (QCT) with DXA-derived parameters in a cohort of thalassaemic patients. Secondarily, we aimed to investigate the role of the two techniques in predicting the risk of fracture.

2 | PATIENTS AND METHODS

2.1 | Patients

This study was conducted according to the Declaration of Helsinki, after approval by the local Ethics Committee.

We retrospectively reviewed a database of patients with β-thalassemia major followed by the Interdepartmental Day Hospital Unit of Thalassemia and Hemoglobinopathies of the Sant'Anna University Hospital in Ferrara. Over a period of 9 years (from January 2010 to December 2019), we included, in the final analysis, patients who had undergone both lumbar and femoral DXA examinations, and abdominal or total-body CT scans with unenhanced acquisition of the lumbar spine, performed for disparate diagnostic issues, within 4 months from the DXA scan.

We collected anthropometric characteristics, including age, height, weight, and sex.

Employing the IT management software SAP of our hospital, we retrieved any spontaneous or fragility fractures occurring from 1 year before up to 5 years after the date of DXA scan at the following sites: thoracic and lumbar spine, ribs, upper and lower extremities (i.e., hands, wrists, feet, ankles), and femurs. In particular, we noted: for thoracic and lumbar spine, fractures at baseline (defined as occurring the year before the date of DXA scan) and those which had occurred during follow-up (corresponding to a maximum of 5 years after the date of DXA scan); for ribs, upper and lower extremities, and femurs, fractures from 1 year before up to 5 years after the date of DXA scan.

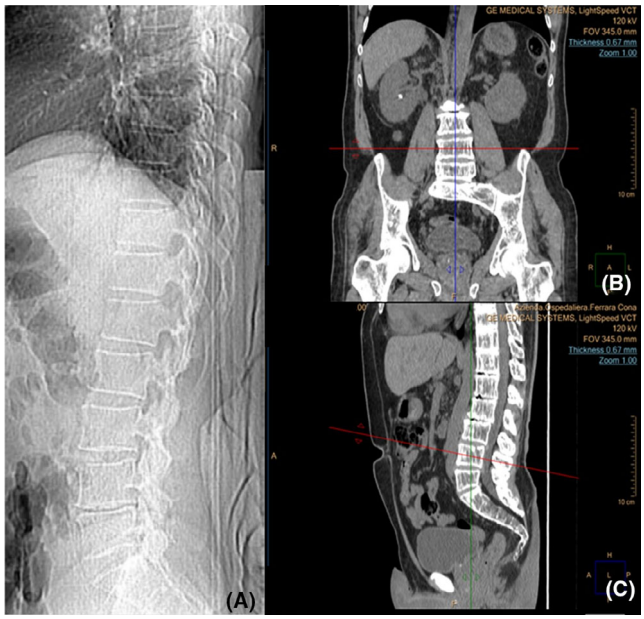

FIGURE 1 Lateral scout view is shown in (A); axes used in phantom-less QCT to detect the middle of vertebral body for BMD assessment are visible in the coronal plane (B) and sagittal plane (C), respectively

Vertebral fractures were classified according to the Genant's semiquantitative method.[9]

All the DXA exams were performed with the same densitometer (Hologic Delphi DXA Scanner, Bedford, MA), and reported according to the guidelines of the International Society for Clinical Densitometry (ISCD) 2019 using T-score or Z-score values as appropriate.

CT examinations were acquired using two different scanners (Lightspeed VCT 64, GE Healthcare, Buckinghamshire, UK; Brilliance iCT 256, Philips Medical Systems, Best, The Netherlands), employing standard acquisition parameters adjusted to patients' biometrics (120–140 kVp, tube load 100–200 mAs depending on automated exposure control system), with 2.5-mm or less slice thickness, soft-tissue kernel and abdomen window.

To define the best predictors of fractures occurring during the follow-up, we considered only one DXA and CT scan for each patient, namely, the exams with the earliest date in order to obtain the longer follow-up length.

2.2 | Phantom-less QCT

CT images of the lumbar spine were examined using the Extended Brilliance Workspace (Philips Healthcare, Cleveland, OH, USA), employing a phantom-less QCT method.

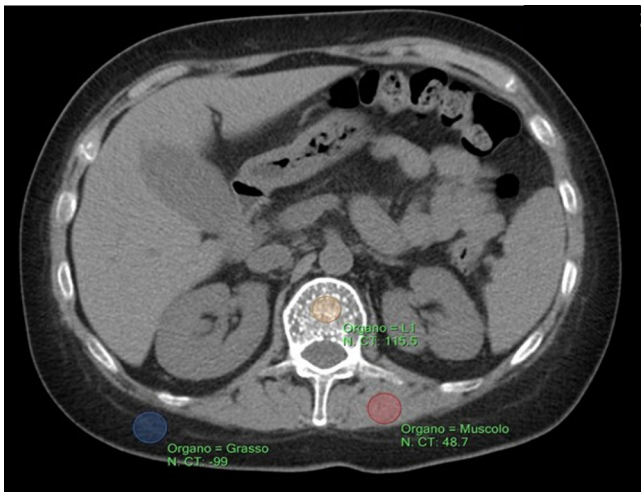

FIGURE 2 Axial CT scan in a patient with Thalassemia major. ROIs for vertebral body (orange circle), paraspinal muscle (red circle) and subcutaneous fat (blue circle) are shown with their respective CT numbers (in Hounsfield Units, HU)

For each patient, unenhanced acquisition was selected for image analysis. Using a lateral scout view, vertebrae of lumbar spine L1–L4 were selected for BMD assessment, avoiding those with abnormalities such as fractures, marked degenerative changes or focal lesions (Figure 1A). Every single slice analyzed on the axial plane for BMD assessment was obtained by employing two axes, both on the coronal plane (blue and red, in Figure 1B) and on the sagittal one (green and red, in Figure 1C) perpendicular to each other, positioning the red one parallel to the vertebral plates and passing through the equator of the vertebral body, and the blue and green ones parallel to the axis of the lumbar spine: the crossing point between the two axes in the two planes corresponded to the mid portion of the vertebral body, consisting only of trabecular bone. Volumetric BMD (expressed in mg/cm^3) was manually calculated by placing a circular region of interest (ROI) on the axial plane in trabecular bone of the middle of vertebral bodies from L1 to L4.

The patient's paraspinal muscles and subcutaneous fat were used as calibration references; thus, additional ROIs were defined for both these tissues (Figure 2).

It has been shown that the results obtained with this method of volumetric lumbar spine BMD assessment are highly reproducible.[10] In our study, for each vertebra, the software converted the CT numbers measured in Hounsfield Units (HU) into equivalent values of volumetric BMD (in mg/cm^3), and calculated T- and Z-scores. Finally, the average of BMD values, T- and Z-scores were calculated, respectively, for the vertebrae included.

T-scores determined by phantom-less QCT are not directly comparable to DXA results. In fact, according to the ISCD guidelines of the International Society for Clinical Densitometry (ISCD) 2019, T-scores are available for BMD assessment only for DXA. For this reason, our volumetric BMD values obtained with QCT were interpreted using the Felsenberg's classification,[11] as suggested by the American College of Radiology (ACR).[12]

TABLE 1 T-score and Z-score by DXA and QCT, expressed as medians with first and third quartiles

Parameter	Method	Median	Quartiles
Lumbar T-score	DXA	−2.90	−4.00/−2.00
	QCT	−2.30	−3.25/−1.05
Lumbar Z-score	DXA	−2.60	−3,80/−1.75
	QCT	−1.30	−2.65/−0.25
Femoral T-score	DXA	−2.60	−3.20/−1.55
Femoral Z-score	DXA	−2.30	−2.85/−1.25

2.3 | Statistical analysis

The results were expressed as mean values ± SD in the case of normally distributed variables, while as medians with first and third quartiles in the case of variables not normally distributed.

For the comparison between T- and Z-scores determined by DXA and QCT (respectively, T_{DXA} and Z_{DXA}, T_{QCT} and Z_{QCT}), parametric tests were used in the case of normally distributed variables (T test for paired or independent samples), while nonparametric ones in the case of variables not normally distributed (Wilcoxon test for paired samples or Mann–Whitney test).

Pearson's correlation coefficient (r) was used when the correlation between the variables satisfied specific requirements (parametric correlations), while Spearman's rho was adopted in the other cases (nonparametric correlations).

The comparison between T- and Z-scores obtained with DXA and QCT, and the correlation between T- and Z-scores and patient age were represented graphically with dispersion diagrams.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each best predictor for risk of fracture, considering diagnostic threshold for osteoporosis ($T_{DXA} = -2.5$ SD and volumetric BMD = 80 mg/cm^3 for lumbar QCT).

A p value <.05 was considered statistically significant. Bonferroni's correction was applied for multiple comparisons.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 19 (IBM Corporation, Armonk, NY, USA).

3 | RESULTS

We included 43 consecutive patients with β-thalassemia major (mean age ± SD: 42.6 ± 8.8 years, range 23–66 years). Among them, 28 were males (mean age ± SD: 44 ± 9; range, 23–66 years), and 15 females (mean age ± SD: 40 ± 8; range, 28–65 years). We analyzed 53 DXA and CT scans performed on the study population.

Comparison between DXA and QCT-derived T- and Z-scores.

In the study cohort, T- and Z-scores are reported in Table 1.

After comparison of lumbar spine T_{DXA} with T_{QCT}, we found that QCT values were significantly higher (i.e., less negative) than those determined by DXA ($p = .002$) (Diagram S1).

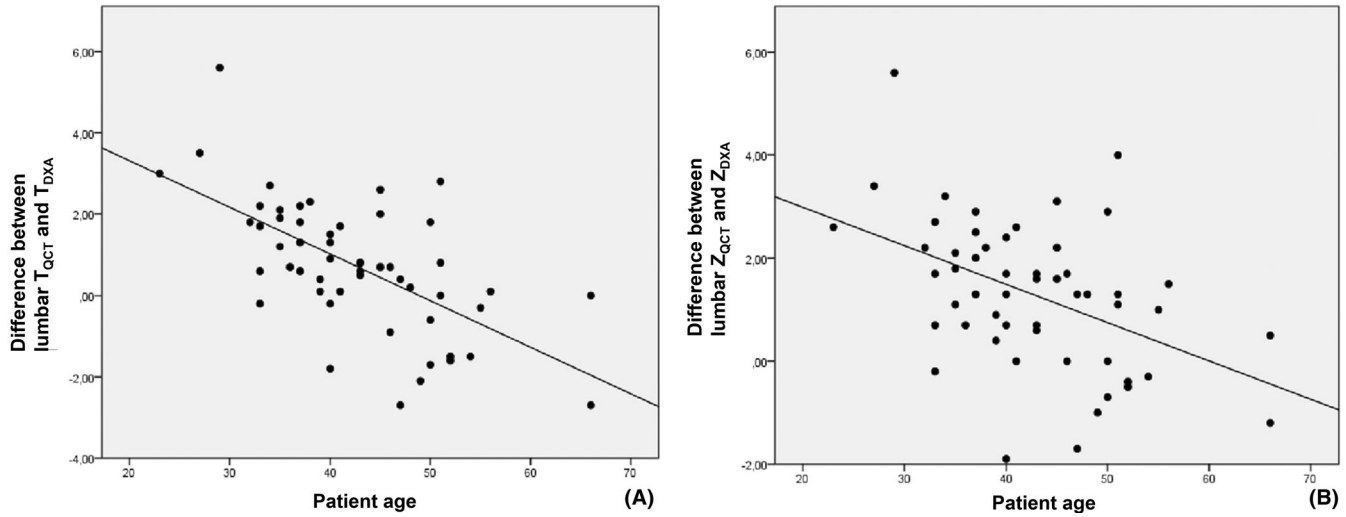

FIGURE 3 (A) Comparison between patient age (x-axis) and the difference between T_{QCT} and T_{DXA} at lumbar spine (y-axis) of the 53 DXA and QCT scans performed on the study population. The regression line, which represents the trend line, going down from top left to bottom right, suggests a negative correlation (r = −0,626). (B) Comparison between patient age (x-axis) and the difference between Z_{QCT} and Z_{DXA} at lumbar spine (y-axis) of the 53 DXA and QCT scans performed on the study population. The regression line, which represents the trend line, going down from top left to bottom right, suggests a negative correlation (r = −0,454)

Similarly, the comparison between lumbar Z_{DXA} and Z_{QCT} showed that QCT provided significantly higher measures (i.e., less negative) than DXA ($p < .001$) (Diagram S2).

The comparison of lumbar T_{QCT} and femoral T_{DXA} showed no statistically significant difference ($p = .248$), whereas lumbar Z_{QCT} were significantly higher than femoral Z_{DXA} ($p < .001$).

In summary, the difference between DXA and QCT-derived T- and Z-scores was found to be statistically significant; in particular, QCT parameters were significantly higher (i.e., less negative) than those determined by DXA.

Correlation of T- and Z-scores with patient age.

The difference between lumbar spine T_{QCT} and T_{DXA} and Z_{QCT} and Z_{DXA} demonstrated a statistically significant association with patient age ($p < .001$ and $p = .001$, respectively; Figure 3A,B). In particular, in our patients aged under 30 years, DXA provided more negative T-scores than QCT, with a difference of 2 units at about 30 years of age. In patients aged 30–50 years, the gap between T-scores obtained with the two methods decreased more and more up to 50 years of age, when this difference was cancelled. In patients aged over 50 years, the aforementioned trend was reversed: QCT provided more negative T-scores than DXA. We also observed the same trend for Z-scores determined by the two techniques.

Comparison between DXA and QCT according to ISCD classification into normal, osteopenic and osteoporotic categories, based on T-score.

The comparison between lumbar spine T_{DXA} according to ISCD classification and ACR classification (based on volumetric BMD) showed the following (Table S1):

- Six patients had normal T_{DXA}. According to the ACR classification, four of them were categorized with normal BMD_{QCT}, whereas 1 patient had osteopenic BMD_{QCT} and one patient had osteoporotic BMD_{QCT} ($p < .001$);
- The 14 patients had osteopenic T_{DXA}. According to the ACR classification, eight of them were classified with osteopenic BMD_{QCT}, whereas four had normal BMD_{QCT} and two had osteoporotic BMD_{QCT} ($p < .001$);
- The 33 patients had osteoporotic T_{DXA}. According to the ACR classification, 21 of them were categorized with osteoporotic BMD_{QCT}, whereas 2 had normal BMD_{QCT} and 10 had osteopenic BMD_{QCT} ($p < .001$).

The comparison between lumbar T_{DXA} and T_{QCT}, using, for both parameters, the ISCD classification into normal, osteopenic and osteoporotic categories (Table S2), showed the following:

- Six patients were categorized with normal BMD_{DXA}. Of these, four showed normal BMD_{QCT}, and two had osteoporotic BMD_{QCT} ($p < .001$);
- 14 patients were classified with osteopenic BMD_{DXA}. Of these, seven had osteopenic BMD_{QCT}, whereas five had normal BMD_{QCT} and two had osteoporotic BMD_{QCT} ($p < .001$);
- The 33 patients were categorized with osteoporotic BMD_{DXA}. Of these, 22 had osteoporotic BMD_{QCT}, while 2 had normal BMD_{QCT} and 9 had osteopenic BMD_{QCT} ($p < .001$).

Comparison between DXA and QCT according to ISCD classification into normal or low BMD, based on Z-score.

The comparison between Z_{DXA} and Z_{QCT} at lumbar spine (Table S3) showed the following:

- The 17 patients were categorized with normal BMD_{DXA}, 16 of whom showed normal BMD_{QCT}, whereas only 1 patient had low BMD_{QCT} ($p = .008$);

- The 36 patients were classified with low BMD_{DXA}, 17 of whom showed low BMD_{QCT}, instead 19 had normal BMD_{QCT} ($p = .008$).

In summary, the difference in terms of classification between DXA and QCT according to the ISCD guidelines into normal, osteopenic and osteoporotic categories, based on T-score, and into normal or low BMD, based on Z-score, was always statistically significant. In particular, DXA provided T- and Z-score values which were more negative than those determined by QCT, and therefore a more pathological classification of bone mineralization.

Prediction of risk of fracture.

In the study population (43 patients):

- The 12 patients had radiographic vertebral fractures (five at baseline, five during follow-up, and two at both baseline and follow-up). Among them, using the semiquantitative method by Genant, in nine patients vertebral fractures were classified as mild, in two patients as moderate and in one patient as severe;
- Five patients had rib fractures;
- One patient had a lower extremity (feet and ankles) fracture;
- No patients had femoral or upper limb fractures.

TABLE 2 Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the best predictive variables for risk of fracture

Parameter	Total fractures			
	Sensitivity	Specificity	PPV	NPV
ACR classification	100%	80%	68%	100%
Femoral DXA T-score	100%	77%	65%	100%
Lumbar QCT T-score	100%	23%	62%	100%

3.1 | Total fracture risk

Among the anthropometric characteristics (age, height, weight, sex), only weight showed a correlation with total fractures ($p = .036$). Particularly, patients with fracture had lower weight than those without fracture. However, this modest association did not remain significant when the Bonferroni's correction was applied, so such a correlation is at least doubtful. For total vertebral fractures, weight did not show any significant correlation.

The association between total fractures and BMD classification based on femoral DXA Z-score and T-score was statistically significant ($p < .001$).

The association between total fractures and BMD classification based on lumbar DXA Z-score was not statistically significant ($p = .156$).

However, the association between total fractures and BMD classification based on lumbar DXA T-score resulted statistically significant ($p = .018$).

The association between total fractures and the ACR classification, based on volumetric BMD obtained by lumbar QCT, was statistically significant ($p < .001$).

The association between total fractures and BMD classification based on lumbar QCT Z-score was also statistically significant ($p < .001$).

Finally, the association between total fractures and BMD classification based on lumbar QCT T-score was statistically significant ($p < .001$).

In summary, all predictive variables considered were significantly correlated with total fractures, excepted for lumbar Z_{DXA}. The most powerful predictive variable for fracture risk was the ACR classification based on volumetric BMD values obtained by QCT. In fact, all patients with fractures presented a BMD_{QCT} compatible with osteoporosis according to this classification, with a 68% prevalence of fractures (13/19). Two other variables came very close in terms of predicting the risk of fracture: femoral T_{DXA} was the second best predictive variable, with a 65% prevalence of fractures (13/20) in the osteoporotic subjects; T_{QCT} was the third best predictive variable, with 62% (13/21) of fractures in the osteoporotic patients.

Sensitivity, specificity, PPV, and NPV of the best predictive variables for fracture risk are reported in Table 2.

3.2 | Vertebral fracture risk

All predictive variables considered were correlated with total vertebral fractures, except for lumbar Z_{DXA}. Also in this setting, we found that the best predictor was the ACR classification. In fact, all patients with fractures presented a BMD_{QCT} compatible with osteoporosis according to this classification, with a 63% prevalence of fractures (12/19). Two other variables came very close in terms of fracture risk prediction: femoral T_{DXA}, with a 60% (12/20) prevalence of fractures, and T_{QCT}, with 57% (12/21) of fractures.

The association between new vertebral fractures and BMD classification based on femoral Z_{DXA} was statistically significant ($p = .031$).

A similar result was found between new vertebral fractures and BMD classification based on femoral T_{DXA} ($p = .008$).

The association between new vertebral fractures and BMD classification based on lumbar Z_{DXA} or T_{DXA} was not statistically significant (respectively, $p = .092$ and $p = .065$).

The association between new vertebral fractures and the ACR classification based on BMD_{QCT} was statistically significant ($p = .005$).

The association between new vertebral fractures and BMD classification based on lumbar QCT Z-score was statistically significant ($p < .001$).

Finally, the association between new vertebral fractures and BMD classification based on lumbar QCT T-score was statistically significant ($p = .013$).

In summary, the predictive variables that proved to be significantly correlated with vertebral fractures appearing during follow-up were: femoral DXA Z-score and T-score, ACR classification, lumbar QCT Z-score and T-score. The best predictive variable for new vertebral fractures was lumbar Z_{QCT} since all patients with fractures had a

TABLE 3 Z-scores and T-scores obtained by DXA and QCT, in patients with and without fractures, reported as medians with quartiles

Parameter	Technique	Fracture	Median	Quartiles	*p* value
Z-score	Femoral DXA	Without	−1.50	−2.22/−0.95	<.001
		With	−2.90	−3.40/−2.40	
Z-score	Lumbar DXA	Without	−2.15	−3.00/−1.05	.016
		With	−3.00	−4.10/−2.60	
Z-score	Lumbar QCT	Without	−0.95	−1.37/0.40	<.001
		With	−2.70	−3.35/−2.10	
T-score	Femoral DXA	Without	−1.85	−2.45/−1.07	<.001
		With	−3.20	−3.70/−2.70	
T-score	Lumbar DXA	Without	−2.30	−3.17/−1.57	.017
		With	−3.10	−4.20/−2.70	
T-score	Lumbar QCT	Without	−1.70	−2.60/0.32	<.001
		With	−3.30	−4.30/−2.75	

Z-score below the expected range (low BMD), with a fracture prevalence of 54% (7/13). While the ACR classification proved to be the second best predictive variable, with a prevalence of 37% (7/19) in patients with low BMD; femoral T_{DXA} was the third best predictor, with 35% (7/20) of fractures.

Considering total fractures, both DXA and QCT-derived Z-scores and T-scores of patients with fractures were significantly lower (i.e., more negative) than those of patients without fractures (Table 3). The same considerations apply to total vertebral fractures and new vertebral fractures.

4 | DISCUSSION

DXA measures still represent the reference standard for the radiological definition of bone mineralization. Another technique for assessing BMD and bone quality, namely QCT, is (re)emerging in the scientific literature and clinical practice, although there is no consensus as to what extent it may substitute or complement DXA in the diagnosis of osteoporosis and assessment of fracture risk.[8]

Despite its widespread use and validation, DXA has well-recognized limitations. Because of its two-dimensional nature due to planar projection, DXA may be biased by bone size, degenerative pathology, and patient positioning.[7] This technique does, in fact, provide measurement of bone area rather than volume, leading to underestimation of bone density in individuals with short stature, a common condition among thalassaemic patients.[7,13] By contrast, axial QCT is a three-dimensional method able to provide volumetric BMD of the spine and proximal femur. Importantly, the phantom-less (i.e., internal calibration-based) approach relies on the use of routine clinical CT data, which have been acquired for other purposes, providing an opportunistic approach to osteoporosis screening while mitigating some drawbacks of QCT, such as higher radiation exposure and costs compared with DXA. This method requires no additional patient time or radiation exposure, and very little time from radiology staff. In particular, internal calibration uses known densities of certain tissues in the image (more often, paraspinal muscles and subcutaneous fat) as a reference to calculate the relation between CT density (expressed in HU) and BMD.[14] The cross-sectional QCT images also allow the accurate identification and consequent isolation of the trabecular bone, which is a more sensitive site for analyzing bone mineral changes than cortical or integral sites.[3,15]

A few studies have previously investigated the role of axial QCT in evaluating thalassemia bone disease.[15–18] In a work by Angelopoulos and colleagues conducted on 13 thalassaemic patients,[15] T-scores and Z-scores obtained by QCT were significantly higher than DXA-derived ones, and this observation is in line with our results. Indeed, we found higher parameters of bone mineralization (i.e., less negative) using QCT in comparison with DXA. However, it should be noted that QCT and DXA-derived T- and Z-scores cannot be used interchangeably. The ACR has provided diagnostic cut points which may be used for assigning a spine QCT diagnostic category, considered approximately equivalent to the WHO guidelines and based on volumetric BMD.[12] The use of T-scores has been avoided in such categorization to underline the fact that QCT spine and hip T-scores are frequently different, and QCT spine T-score may overestimate a patient's risk of fracture in the general population.

Accordingly, Mylona and colleagues found that the overall prevalence of osteoporosis was 44% with DXA and 6% with QCT in 48 patients.[18] This may be partly explained by the relatively short stature of thalassaemic patients, which might affect the results of BMD when using DXA, since such values are known to depend on both bone mineral content and bone size. Hence, the low bone density obtained may simply reflect the short stature of such patients.[19] Moreover, the same authors employed high resolution computed tomography (HRCT) to evaluate the cortex integrity and the number and thickness of trabeculae. Using the trabecular number as an indicator of osteoporosis, they concluded that QCT may evaluate thalassemic osteopathy better than DXA.

In our study, the absolute difference between lumbar T- and Z-scores provided by DXA and QCT demonstrated a strong correlation with patient age. The delayed bone age, as already mentioned, is a

peculiar morpho-structural characteristic of young thalassaemic patients, so that they should not be directly compared with the unaffected general population: we hypothesize that lumbar Z_{DXA}, employed for BMD assessment in females prior to menopause and in males aged <50 years according to the ISCD guidelines, may result excessively negative because of the comparison between the reference data (age, gender and ethnicity peers) and normal size for their chronological age. On the contrary, in our patients aged ≥50 years, DXA provided less negative lumbar T-values than those determined by QCT, most likely because DXA is more susceptible to degenerative changes, such as osteophytes and soft tissue calcifications (i.e., aortic calcification), that tend to falsely increase BMD calculation in DXA scans.

While exploring the predictive role for fracture risk of DXA and QCT variables, we found that, considering both total and vertebral fractures, the strongest predictor was the ACR classification based on volumetric BMD quantified by QCT.

The prevalence of fracture among all patients with thalassemia is reported to be approximately 16%.[20] In the study cohort, the spine was the most frequently involved site, and vertebral fractures were mainly classified as "mild" according to the semiquantitative method described by Genant. This is in contrast with previous reports, in which fractures were considered more common in the upper extremities.[21]

Previous studies have documented that, in the general population and at least in males, QCT may be more predictive for vertebral fractures than lumbar DXA.[22–25] Obviously, in elderly patients, degenerative changes of the spine, aortic calcification, or even unrecognized mild vertebral fractures may interfere with DXA interpretation, whereas cortical and trabecular bone can be accurately separated with QCT, since the latter is largely independent of degenerative pathology.[25] Indeed, we observed that the definition of osteoporosis based on QCT showed high sensitivity (100%), specificity (80%) and NPV (100%), and good PPV (68%) for fracture identification.

We believe that QCT is valuable in specific clinical scenarios to assess bone mineralization and mechanical competence in metabolic bone disease; notably, in the future, this technique could play a major role in conditions where trabecular bone deterioration is prominent, such as in β-thalassemia. However, this study carries certain limitations, above all the retrospective study design and limited number of patients. We acknowledge that the retrospective analysis of existing CT data should be treated with some caution, in spite of strict quality controls on the stability of CT scanners adopted in our Institution. We did not consider different treatments adopted in our study cohort. A previous study[16] has proposed that BMD measurement by QCT may be unreliable in inadequately chelated patients, since iron deposition may result in increased X-ray attenuation values of trabecular bone,[17] but this was not the case of our population.

Further studies with larger cohorts are needed to explore the effective role of QCT in assessing bone health in thalassaemic patients, and predicting the risk of fracture in this unique population.

5 | CONCLUSIONS

In a population of thalassaemic patients, DXA provides more negative measures than those determined by phantom-less QCT, and therefore a more pathological classification of bone mineralization. However, it seems that QCT may evaluate osteopathy better than DXA in these specific settings, since volumetric BMD would seem to have a stronger predictive role for fracture risk than DXA scans. We believe that, in the future, QCT could play a major role in conditions where interest is focused on trabecular bone deterioration, such as in β-thalassemia. Findings from this study could suggest the use of opportunistic phantom-less QCT, derived from routine abdominal CT scans, as an integrative tool in clinical practice, to obtain a comprehensive radiological evaluation of thalassaemic osteopathy using simple PACS measurement tools and a modest amount of time.

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CONFLICT OF INTEREST

The authors declares there is no potential conflict of interest.

DATA AVAILABILITY STATEMENT

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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