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Low bone mineral density and its influencing factors in spinal muscular atrophy without disease-modifying treatment: a single-centre cross-sectional study

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Abstract

Background Children with spinal muscular atrophy (SMA) are at risk of low bone mineral density (BMD) and bone fragility. This study aims to assess lumbar spine BMD measured by quantitative computed tomography (QCT) and investigate influencing factors of low BMD in children with SMA without disease-modifying treatment.

Methods Demographic data, laboratory parameters, QCT data, and data on spinal radiographs were collected. A linear regression model was carried out to explore the correlations between BMD and its related factors.

Results Sixty-six patients with SMA who had complete records between July 2017 and July 2023 were analyzed, with SMA with a mean age of 5.4 years (range, 2.4–9.7 years), including type 1 in 14, type 2 in 37, and type 3 in 15. 28.8% of patients (19/66) were diagnosed with low BMD (Z-scores ≤ − 2), and the mean BMD Z-scores on QCT was − 1.5 ± 1.0. In our model, BMD Z-scores was associated with age (β=-0.153, $p = 0.001$). SMA phenotype and serum bone metabolism markers, such as serum phosphorus (P), alkaline phosphatase (ALP) and 25-Hydroxyvitamin D (25-OH-D) levels did not independently predict low BMD. ROC analysis showed that the age ≥ 6.3 years predicts a Z-scores ≤ -2.0 with a sensitivity of 68.4% and a specificity of 68.1%.

Conclusions Low BMD were highly prevalent in children with SMA without disease-modifying treatment in our centre. Regular monitoring of BMD is necessary for all types of SMA children, especially those aged ≥ 6.3 years.

Keywords Spinal muscular atrophy, Quantitative computed tomography, Bone mineral density, Infuencing factors, Children

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Introduction

Spinal muscular atrophy (SMA) is an inherited genetic disorder affecting the motor neurons, leading to muscle weakness and wasting. It is caused by homozygous absence by deletion or gene conversion events (90%), hybrid genes (5%), or subtle disease-causing variants (<5%) of the survival motor neuron 1 (SMN1) gene [1, 2]. SMA ranges from severe types with early onset to milder forms that may not be apparent until adulthood.

Children with any kind of motor disabilities are susceptible to developing pathologically low bone mass and fragility fractures [3]. Skeletal system abnormalities are crucial factors in limiting the quality of life of children with SMA. Consequently, there has been a growing emphasis on assessing bone health status as an essential component of SMA management in recent years. Recent SMA guidelines recommend that SMA patients should be followed up with annual routine whole spine X-ray for scoliosis detection and dual-energy X-ray absorptiometry (DXA) scan monitoring of bone mineral density (BMD) [4]. However, DXA is a two-dimensional imaging technique that may not accurately reflect the three-dimensional structure and true volumetric bone density of the skeleton, especially when measuring the long bones and hip bones of children or patients with short stature, it may underestimate bone density [5]. Age-matched, height, bone age, or bone size are often used to adjust BMD Z-scores obtained by DXA to get closer to the actual BMD [6–9]. In addition, DXA tends to overestimate BMD in patients with spinal rotation or scoliosis due to the overprojection effect, resulting in inaccurate BMD measurements [10–12]. However, progressive scoliosis due to deteriorating axial muscle strength is one of the most important complications occurring in virtually all children with SMA type 2 and a significant number with type 3 [13]. In contrast, quantitative computed tomography (QCT) can measure the true volumetric BMD at the lumbar trabecular bone without any limitations due to its direct measurement. As the parameter is three-dimensional, volumetric BMD can reflect actual bone mineral content in growing subjects or smaller individuals. Previous studies have confirmed the application value of QCT in evaluating BMD in pediatric patients [14–16], but no cases have been reported in SMA.

The published literature has documented bone density data, fracture incidence, and treatment options for children with SMA in various regions, including the UK, USA, Italy, and China [17–21]. In SMA patients, bone health is negatively affected by factors such as an intrinsic bone defect, the lack of weight-bearing activity, and muscle weakness. To our knowledge, only one study investigated the BMD based on DXA and explored the influencing factors in children with SMA types 2 and 3, and showed that phenotype and serum parathyroid hormone (PTH) level might be the influencing factors of BMD [21]. Thus, the degree and extent of poor bone health among Chinese patients with SMA are not fully understood or discussed.

Therefore, this study aimed to examine BMD values measured by QCT and further identify the factors that contribute to low BMD in SMA patients at our centre.

Materials and methods

Study participants

We conducted a review of patients with confirmed diagnoses of SMA at the West China Second Hospital of Sichuan University between July 2017 and July 2023. The diagnosis of SMA is clinically and genetically confirmed for all patients, ranging from newborn to 18 years old. If patients had enrolled in a therapeutic clinical trial or started using new drugs (e.g. nusinersen) they were censored on the day of enrollment or the first day of therapy. In additions, patients with rickets should be excluded. Thus, our analyses were based on data from patients without disease-modifying treatment.

The study involving human subjects was approved by the Ethics Committee of the West China Second University Hospital, Sichuan University (20200021gc). The informed consent of all patients was obtained, and all patients agreed to participate in the study.

Data collection

Data extracted from the electronic medical records included demographic data (age, age of onset, age of diagnosis, sex, height and weight), disease characteristics, ambulation status, laboratory parameters, previous fractures, scoliosis and BMD values. Age- and sex-specific weight and height percentiles were calculated based on the growth charts for Chinese children and adolescents. Short stature and underweight were defined as a height and weight below the 3rd percentile of the reference, respectively. The results of laboratory tests including serum calcium, phosphorus, alkaline phosphatase (ALP), serum level of Vitamin D, and PTH were collected. The SMA classification system was used to define SMA phenotypes based on age at symptom onset and maximal motor milestones, with modifications previously published to distinguish SMA 1a−1c, SMA 2a−2b, and SMA 3a−3b [4, 22].

Lumbar BMD measured by QCT

A Neusoft 128-slice helical CT (NeuViz128, China) was used to acquire the CT imaging of the lumbar spine. Asynchronous BMD calibration in combination with the QCT Pro analysis software (version 4.2.3; Model 3 QA phantom; Mindways Software, Inc.) was used to extract the trabecular volumetric BMD (mg/cm^3) at the lumbar spine (L1–L4) (Fig. 1). The QCT software manufacturer

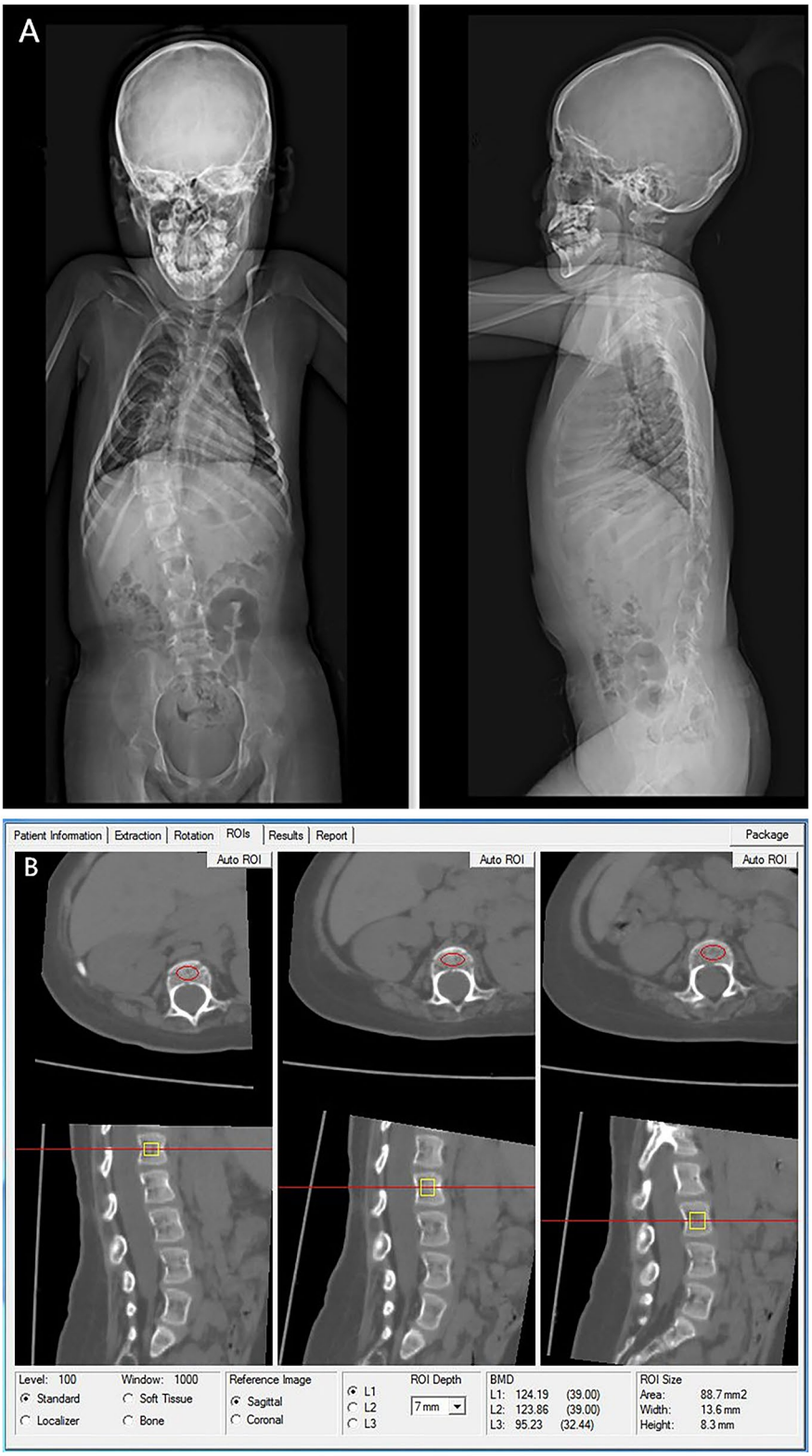

Fig. 1 A 7-year-old girl with SMA type 2. (**A**) Routine plain radiography of the spine shows a thoracolumbar scoliosis. (**B**) The measurements of L1, L2, and L3 vertebral trabecular volumetric bone mineral density (BMD) are shown. The BMD of L1, L2, and L3 are 124.19 mg/cm^3, 123.86 mg/cm^3, and 95.23 mg/cm^3, respectively; the average lumbar volumetric BMD is 109.31 mg/cm3, and the Z score is -2.02

(Mindways Software) provided the reference values for vertebral BMD Z-scores based on age and gender [23]. According to the recommendations of the International Society for Clinical Densitometry for children, a Z score lower than 2.0 is defined as a low BMD [24]. In this study, the time interval between QCT examination and the measurements or assessments of other variables is less than two weeks.

Statistical methods

Data distribution was assessed with a Kolmogorov-Smirnov test. To describe quantitative data with a normal or symmetrical distribution, the mean ± standard deviation values were utilized; and the median (P25, P75) was used to describe data with a non-normal distribution. Two group comparison variances between normal and non-normal distributions were analyzed using the Student's t-test and Mann-Whitney U-test. Single-factor analysis of variance (ANOVA) was performed for multiple group comparisons. The qualitative variables according to the number of samples were performed by chi-square test or Fisher's exact test. Pearson and Spearman correlations were used to assess the correlation between BMD Z-scores and different variables. A multiple linear regression model was carried out to assess the factors predictive of low BMD Z-scores. Finally, a Receiver Operator Characteristic (ROC) curve analysis was computed to find optimal cut-off points for age to predict a low BMD (Z-scores ≤ -2.0). Statistical significance was defined as $p<0.05$, two-sided. The SPSS software (version 23.0, IBM Corp., Armonk, NY, USA) was used to process the data.

Results

Demographic data and clinical characteristics

In this study, 66 patients with a confirmed diagnosis of SMA were included. Table 1 shows the characteristics of the sample by SMA subtype. In all, 14 SMA type (1a=2,1b=2,1c=11), 37 SMA type 2 (2a=24, 2b=14) and 15 SMA type 3 (3a=8, 3b=5). The sex distribution

Table 1 Demographics and BMD data of patients with SMA

	Overall	SMA 1	SMA 2	SMA 3	*P*
Number	66	14	37	15	
Male(%)	35(53.0)	5(35.7)	22(59.5)	8(53.3)	0.317
Age (years)	5.4(2.4,9.7)	2.0(0.6,4.9)	5.7(2.4,9.2)	11.6(7.3,14.9)	< 0.05
Age of onset (years)	1.0(0.6,1.5)	0.4(0.2,0.5)	1.0(0.7,1.2)	3.0(1.5,3.1)	< 0.01
Age of diagnosis (years)	2.3(1.1,6.4)	0.5(0.3,1.3)	2.3(1.3,6.7)	6.0(3.1,13.0)	< 0.01
Short stature	17(25.8)	2(14.3)	12(32.4)	3(20.0)	0.335
Underweight	23(34.8)	6(42.8)	14(37.8)	3(20.0)	0.346
SMN2 copies					
1	1	1	0	0	
2	10	5	3	2	
3	28	4	17	7	
4	4	1	0	3	
NR	23	3	17	3	
lumbar spine BMD (mg/cm^3)	131.4 ± 29.5	141.2 ± 23.1	127.8 ± 29.8	131.4 ± 29.5	0.207
Z-scores	-1.5 ± 1.0	-1.1 ± 0.8	-1.6 ± 1.0	-1.5 ± 1.2	0.197
≤−1.5(%)	30(45.5)	4(28.6)	21(56.7)	6(40.0)	0.164
≤−2(%)	19(28.8)	1(7.1)	13(35.1)	5(33.3)	0.084
Ca (mmol/L)	2.4 ± 0.1	2.5 ± 0.1	2.4 ± 0.1	2.2 ± 0.1	0.842
P (mmol/L)	1.7 ± 0.3	1.8 ± 0.2	1.7 ± 0.3	1.8 ± 0.4	0.308
ALP(U/L)	166.7 ± 45.5	159.6 ± 45.2	171.0 ± 41.9	162.4 ± 55.6	0.710
Elevated serum Ca	1(1.5)	1(7.1)	0	0	
Low serum P	8(12.1)	1(7.7)	6(17.6)	1(7.1)	
Low ALP	17(25.8)	4(33.3)	10(29.4)	3(21.4)	
25-OH-D(ng/mL)	17.4(12.6,25.5)	20.4(17.1,27.4)	19.0(11.5,28.5)	12.8(9.8,20.5)	0.042
20–30 ng/mL	14(21.2)	5(35.7)	7(18.9)	2(13.3)	
≤ 20 ng/mL	4060.6)	7(50.0)	21(56.8)	12(80.0)	
Scoliosis(%)	30(45.5)	5(35.7)	18(48.6)	7(46.7)	0.221
Dislocation of the hip(%)	25(37.9)	7(50.0)	15(40.5)	3(20.0)	0.706
Non-ambulant(%)	47(71.2)	14(100)	29(78.4)	4(26.7)	0.000
Long bone fractures(%)	3(4.5)	0	3(8.1)	0	

BMD=bone mineral density, SMA=spinal muscular atrophy, QCT=quantitative computed tomography, SMN2=survival motor neuron gene 2, NR=not reported, ALP=alkaline phosphatase, 25-OH-D=25-Hydroxyvitamin D

was similar across SMA subtypes. Age of onset, age of diagnosis and age differed significantly by SMA subtype, youngest in SMA1 and oldest in SMA3 groups, consistent with the onset of symptoms leading to SMA diagnosis. The short stature and underweight represented about 25.8% and 34.8%, respectively. Similarly, up to 45.5% (30/66) and 37.9% (25/66) of patients presented scoliosis and dislocation of the hip, respectively. None of the 66 children had vertebral fractures. Three patients (4.5%) had histories of long bone fractures.

The serum phosphate was slightly above the normal range in 2 children (3.0%) and slightly below the normal range in 8 children (12.1%). The serum Ca was slightly above the normal range in only one child (1.5%), and the ALP levels were in the normal range in the 49 children (74.2%). There was no significant difference in levels of serum Ca, P and ALP between the three SMA subtypes ($p>0.05$). We did not tabulate data about PTH because this data was too incomplete. Among the 66 children, 81.8%(54/66) had 25-OH-D within the lower range of normal value (≤30 ng/mL); 40 patients (60.6%) had vitamin D deficiency (≤20 ng/mL), and 14 children (21.2%) had insufficiency (range, 20–30 ng/mL).

Assessment of lumbar spine BMD

QCT scans showed that the trabecular BMD of the lumbar spine was low. The mean volumetric BMD was 131.4±29.5 mg/cm^3, and the mean BMD Z-scores was −1.5±1.0 (range −3.68 to 0.7). 28.8% (19/66) children were diagnosed with low BMD (Z-scores≤−2), and 47.0% (31/66) of children had BMD with Z-scores≤−1.5. For SMA type 1 children, 7.1% (1/14) of them were diagnosed with low BMD. For SMA type 2 and 3, 35.1% (13/37) and 33.3% (5/15) were diagnosed with low BMD, respectively. Table 2 provides the details of the associations between BMD Z-scores and presenting clinical factors.

Table 2 Comparison of normal and low BMD by Z-scores in patients with SMA

	Normal BMD (*n*=47)	**Low BMD (*n*=19)**	***P***
Male(%)	23(48.9)	12(63.2)	0.295
Age (years)	5.1(1.7,7.5)	9.3(3.8,11.6)	0.050
0–5 (years)	23(48.9)	6(31.6)	0.272
5–10(years)	15(31.9)	6(31.6)	
≥ 10(years)	9(19.1)	7(36.8)	
Age of diagnosis (years)	2.1(0.7,5.2)	2.6(1.2,8.2)	0.257
Age of onset (years)	1.0(0.5,1.5)	1.2(0.7,1.6)	0.065
Short stature	14(29.8)	3(15.8)	0.386
Underweight	18(38.3)	5(26.3)	0.355
SMN2 copies, n			0.576
1	1	1	
2	8	2	
3	19	9	
4	2	2	
ND	17	6	
Ca (mmol/L)	2.5 ± 0.1	2.4 ± 0.1	0.065
P (mmol/L)	1.7 ± 0.3	1.8 ± 0.3	0.469
ALP(U/L)	161.9 ± 43.1	178.9 ± 50.4	0.194
25-OH-D(ng/mL)	18.0(14.5,26.7)	16.0(11.1,22.9)	0.411
> 30 ng/mL	9(19.1)	3(15.8)	0.944
20–30 ng/mL	10(21.3)	4(21.1)	
≤ 20 ng/mL	28(59.6)	12(63.2)	
Scoliosis(%)	19(40.4)	11(57.9)	0.197
Dislocation of the hip(%)	17(36.2)	8(42.1)	0.653
Non-ambulant(%)	35(74.5)	12(63.2)	0.358
Long bone fractures(%)	1(5.3)	2(4.3)	0.861
SMA phenotype			0.084
1	13(27.7)	1(5.3)	
2	24(51.1)	13(68.4)	
3	10(21.3)	5(26.3)	

BMD=bone mineral density, SMA=spinal muscular atrophy, QCT=quantitative computed tomography, SMN2=survival motor neuron gene 2, NR=not reported, ALP=alkaline phosphatase, 25-OH-D=25-Hydroxyvitamin D

Table 3 Multivariate analysis to find out the predictors of low BMD (Z-scores≤-2) in patients with SMA

Predictors	Unstandardized coefficients (β)	95% CI for β		t	*P*
		Lower	Upper		
(Constant)	0.716	-1.608	3.039	0.618	0.539
SMA Phenotype					
SMA 1	0				
SMA 2	0.071	-0.623	0.764	0.205	0.839
SMA 3	0.715	-0.239	1.669	1.503	0.309
25-OH-D(ng/mL)					
> 30 ng/mL	0				
20–30 ng/mL	-0.048	-0.9052	0.809	-0.113	0.911
≤ 20 ng/mL	0.371	-0.481	1.220	0.872	0.387
Age (years)	-0.153	-0.234	-0.073	-3.812	0.001
P (mmol/L)	-0.581	-1.473	0.310	-1.308	0.196
ALP(U/L)	-0.002	-0.007	0.004	-0.576	0.567

R-value for model = 0.540; F = 3.06; *P* = 0.009 (analysis of variance)

BMD = bone mineral density, SMA = spinal muscular atrophy, 25-OH-D = 25-Hydroxyvitamin D, ALP = alkaline phosphatase, CI = confidence interval

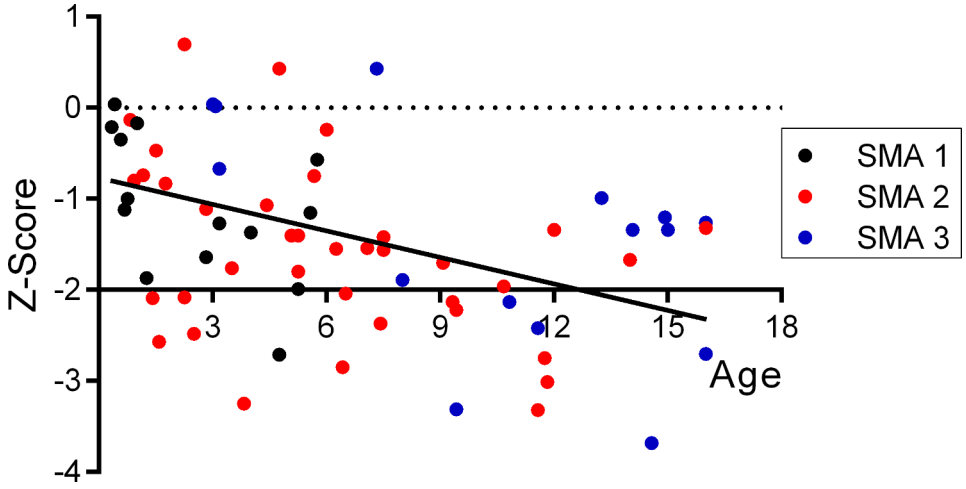

Fig. 2 The scatter plot showed a negative significant correlation between age and BMD Z-scores (r=-0.443, p = 0.001)

Influencing factors of BMD Z-Scores

Age, SMA phenotype and serum bone metabolism markers (P, ALP, 25-OH-D) were evaluated with a linear regression model (Table 3). It was found that age had a significant association with the BMD Z-scores in patients with SMA (β=-0.153, p=0.001). The variance inflation factor was assessed for multicollinearity and found to be insignificant (<5). A significant negative correlation was found between age and BMD Z-scores as shown in the scatter plot in Fig. 2 (r=-0.443,p=0.001).

Because we observed that age contributes significantly to low BMD, We determined the cut-off value of this factor to suggest a diagnostic value and to estimate the risk of low BMD. The ROC age curve identified a cut-off point of ≥6.3 years of age; this age predicts a Z-scores ≤ -2.0 with a sensitivity of 68.4% and a specificity of 68.1%.

Discussion

In patients with SMA, obtaining accurate measurements of BMD by DXA is usually difficult. Severe spinal rotation, scoliosis, and other musculoskeletal changes are the most frequent causes of this difficulty. Lee et al. [10] proved that DXA tends to underestimate lumbar osteoporosis in patients with Duchenne muscular dystrophy who also have scoliosis when comparing DXA results with QCT results. In addition, QCT offers more accurate measurements than DXA, which can be affected by spinal deformities or other musculoskeletal changes [14]. Children with SMA have a high prevalence of scoliosis, with an incidence of 60–90% and an initial presentation in early childhood [13]. Nevertheless, QCT software can directly correct scoliosis curves and measure trabecular bones with accuracy. Therefore, this study is important because it is the first one to examine the factors that contribute to low BMD in patients with SMA using QCT data.

In this study, we found that low BMD was prevalent in children with SMA in mainland China. Up to 28.8% (19/66) of patients had lumbar spine BMD Z-scores ≤ -2 obtained by QCT and 47.0% (31/66) of patients had Z-scores ≤ -1.5. In 2012, Poruket al. [25] found that the mean values of lumbar spine BMD were much lower than those of healthy controls of similar age in 47 patients with SMA type 1. Wasserman et al. [19] reported a reduction in BMD measured with DXA (height adjusted Z-scores ≤ -2) in 85% (53/62) of children with SMA type 1–3 in USA, which was greater than that we observed in our study. This might be related to the older age of patients included in their study. Additionally, in Baranello et al. [20], 15.6% (5/32) of the patients with SMA type 2–3 were diagnosed with low BMD based on DXA, while in Peng et al. [21], the percentage was 67.5% (27/40). Artifacts caused by scoliosis, which is common in children with SMA, could also contribute to the false positive results in measured BMD. This highlights the complexity of DXA interpretation and the limitations of BMD assessment by DXA in this particular group of children. It is necessary to explore other novel imaging modalities as part of bone health assessment. Nevertheless, the prevalence of low BMD in patients with SMA is quite high, requiring immediate clinical attention.

Our findings suggest that age might be a useful indicator for assessing the risk of low BMD of the lumbar spine in patients with SMA (β=-0.153, $p=0.001$). Even young subjects affected by SMA should be considered at risk of low BMD. It is not unexpected that age is the factor associated with low BMD, as SMA children may not be able to increase bone mass through exercise and physical activity compared to healthy children, leading to a progressive bone mass deficient state. A previous cross-sectional study involving twelve SMA patients also found that young children had BMD Z-scores within the normal range, while teenagers had lower Z-scores [18]. Their analysis revealed that age had a more significant effect on BMD than disease severity or ambulatory status. Wassermann et al. [19] observed that lumbar BMD Z-scores significantly decreased with age, irrespective of SMA subtype. An ROC age curve analysis was further conducted in our study. The finding may be applicable for guiding bone care in patients with SMA at age≥6.3 years, which is an indicator of low BMD. We believe that BMD should be assessed as early as the diagnosis of SMA is completed, or beyond this age cut-off value, and monitored at regular intervals according to the latest International Management Consensus [4].

Vitamin D plays a crucial role in maintaining the health of the skeletal system. It mediates the mineralization of newly synthesized osteoid tissue within bone. In our study, we observed that vitamin D deficiency and insufficiency were found in 81.8% of SMA patients, consistent with the findings of the study in other countries [26]. Notably, vitamin D can promote intestinal Ca and P absorption and maintain a balance in calcium metabolism. Vitamin D deficiency stimulated PTH secretion and PTH increased bone resorption to maintain calcium homeostasis. In our study, we observed that the levels of serum Ca, P and ALP were mostly within normal ranges in children of SMA. This phenomenon is also consistent with previous studies [17, 21, 27]. Therefore, based on our statistical model, prediction of BMD Z-scores was not possible with the serum P (β=-0.581,$p=0.196$) or ALP (β=-0.002,$p=0.567$) level. We do not recommend routine serum Ca, P or ALP screening in SMA children with low BMD to increase disease burden. In addition, we did not observe any contribution of vitamin D insufficiency and deficiency (vs. normal) to BMD Z-scores loss. We observed that there were statistically significant differences in 25-OH-D between the three SMA phenotypes. The level of 25-OH-D tended to decrease with the change of SMA subtypes from 1 to 3. Patients with SMA 3 had significantly lower 25-OH-D than those with SMA 1 ($p=0.04$). A previous study has shown that for SMA patients, increased vitamin D and calcium consumption were associated with an increase in BMD [26]. Therefore, providing children with SMA with sufficient daily calcium and vitamin D intake is crucial, even if they don't show an increase in PTH levels or bone markers.

The association of SMA phenotype with BMD outcome is controversial [19, 21, 28]. A recent study of Chinese children with SMA showed that BMD Z-scores tended to increase with the change of SMA subtypes from 2a-3b. In our study, we observed that children with SMA type 2 had lower lumbar BMD Z-scores than those with SMA type 3, but no significant difference. In addition, we found that the proportion and the mean of BMD Z-scores in the study of Peng et al. were significantly lower compared to our study. This may be consistent with the known effect that DXA underestimates volumetric bone density in those with small bone size [29]. Our study may shed light on the complexity of BMD in SMA patients, which may be influenced by multiple factors other than disease severity alone. In addition, the lifestyle and daily activities of SMA patients may not differ significantly between different types, which could reduce the impact of SMA type on BMD measurements. To explain how bone and muscle interact in children with neuromuscular diseases, a model for muscle-bone interactions has been introduced [30]. The absence of SMN protein also has a significant effect on BMD. In mouse models, SMN protein indirectly activates osteoclasts by interacting with cell signaling molecules such as osteoclast stimulating factor 1 (OSTF1) and plays an important role in bone development and bone resorption activity [31, 32]. Therefore, the high incidence of low BMD in SMA patients may be one

of the primary symptoms of the disease itself, and may not simply be attributed to muscle weakness and lack of exercise [33]. Moreover, our study may suggest a nonlinear or threshold effect in the relationship between BMD Z-scores and SMA type, where the impact of SMA type on BMD may not be significant before certain age groups or stages of the disease. Therefore, we recommend that future studies should consider larger and more diverse samples, as well as more comprehensive assessments of potential confounding factors.

The strength of this study is that the lumbar spine BMD obtained by QCT is more accurate than the DXA method. Our study has several limitations. Firstly, some of our analyses may have been underpowered because of the small number of participants. Secondly, at our centre, patients with spinal muscular atrophy (SMA) are generally recommended to undergo annual QCT tests to monitor changes in BMD. Although the radiation dose of QCT is higher than the DXA, the effective dose of a single QCT examination is only approximately 1.5 mSv, and the radiation dose is at a low level and safe for SMA patients. Thirdly, this study is based on existing medical records or databases, and historical measurement data for PTH may not be available. Patients' dietary history and calcium intake, as well as detailed vitamin D treatment, were also not available, which could also affect their bone health. Future prospective studies should include a larger multicenter population and a more comprehensive collection of the data for evaluation. However, because this rare disease of bone health publications is limited, this is still a valuable complement to existing literature.

Conclusion

In conclusion, low BMD was common among children with SMA who did not receive disease-modifying treatment in our centre. Regular BMD monitoring is necessary for all types of SMA children, especially those aged≥6.3 years. So that early diagnosis and appropriate intervention can be planned to prevent the complications related to low BMD.

Abbreviations

SMA	Spinal Muscular Atrophy
DXA	Dual-energy X-ray Absorptiometry
BMD	Bone Mineral Density
QCT	Quantitative Computed Tomography
SMN	Survival Motor Neuron Gene
ALP	Alkaline Phosphatase
25-OH-D	25-Hydroxyvitamin D

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Not applicable.

Author contributions

CL had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Study design and concept: CL and HQ. Acquisition, analysis, or data interpretation: CL, DY, LL, XM, and XC. Drafting of the manuscript: CL. Statistical analysis: CL and DY. Study supervision: GN and HQ. The authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study involving human subjects was approved by the Ethics Committee of the West China Second University Hospital, Sichuan University (20200021gc). The informed consent of all patients was obtained, and all patients agreed to participate in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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