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POSTER ABSTRACTS

114.SICKLE CELL DISEASE, SICKLE CELL TRAIT AND OTHER HEMOGLOBINOPATHIES, EXCLUDING THALASSEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Association between Low Bone Mineral Density and Pain in a Prospective Cohort of Adults with Sickle Cell Disease: Preliminary Results from the SCD Bone Pain Study

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Background:
Osteonecrosis (ON), a prevalent skeletal complication of sickle cell disease (SCD), typically associates with severe chronic pain, frequent acute care utilization, and permanent disability. We previously showed that low bone mineral density (BMD) independently associates with hip ON and chronic pain in a pediatric SCD cohort. We now present preliminary data on the association between low BMD and pain in a prospective cohort of adults enrolled in the SCD Bone Pain Study (NCT05283148).
Methods:
Written informed consent was obtained from all participants, who were recruited from ambulatory adults with SCD seen at the University of California Davis Comprehensive Cancer Center. All participants underwent dual-energy X-ray absorptiometry (DXA) scans of their lumbar spine, left hip, and left forearm. Vertebral fractures were assessed by thoracolumbar morphometry in the DXA scanner. All participants also completed the Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) Pain Impact questionnaire. We used linear regression to evaluate the association between ASCQ-Me pain scores and low BMD (categorically defined as BMD Z-score $\leq$ -2 at any DXA site). We also used linear regression to determine the association between ASCQ-Me pain scores and continuous total hip and lumbar spine BMD Z-scores. Lastly, we evaluated the impact of other covariates on pain scores, with low BMD or BMD Z-scores included in the least absolute shrinkage and selection operator (LASSO, no shrinkage).
Results:
Thirty adults (median age 34.5 years [20-67 years]) completed the study between Nov 2022-Jul 2023. Baseline characteristics are summarized in Table 1. There was a borderline significant association between low BMD and lower (worse) pain scores (p=0.077). Continuous BMD Z-scores of the total hip (p=0.081) and lumbar spine (p=0.024) were independently associated with higher (better) pain scores. In addition to low BMD, only white blood cell count (WBC), indirect bilirubin, and vitamin D were identified as possible covariates (all had non-zero coefficients in LASSO analysis). Low BMD was significantly associated with pain (p=0.024), even after adjusting for WBC, indirect bilirubin, and vitamin D (Table 2). Similarly, we found that higher hip (p=0.059) and lumbar (p=0.027) BMD Z-scores were associated with higher (better) pain scores, despite adjusting for the same confounders.
Discussion:
We found low BMD in 12 of 30 (40%) adults enrolled in the SCD Bone Pain Study. Like other chronic hemolytic anemias, compensatory increased erythropoiesis leads to trabeculae degradation, cortical bone thinning, and eventual low bone mass. Lumbar vertebrae comprises mostly of trabecular bone, while the hip joint has mostly cortical bone. This might explain why mean lumbar BMD Z-scores were lower than hip BMD Z-scores (Table 1), and why lumbar spine BMD Z-scores directly and significantly correlated with pain scores (Table 2). These preliminary data suggest that pain is more prevalent in SCD adults with low BMD than those with normal BMD as we previously reported in a pediatric SCD cohort.
Pain scores decrease (worsen) with increasing WBC, which suggests an inflammatory component to chronic SCD pain. Contrary to expectation, higher indirect bilirubin (a marker of increased hemolysis) significantly correlated with higher (better) pain scores. Similarly, higher vitamin D (a proxy for bone health) correlated with lower (worse) pain scores, though this association

was non-significant. The reason(s) for these counterintuitive associations between pain scores, indirect bilirubin, and vitamin D levels is currently unknown.
Limitations include a small sample size, though using the LASSO method for multivariate regression adjusted for this. Further, low BMD causality could not be determined at this time. Recruitment is ongoing with an enrollment target of 50 adults with SCD by Nov 2023. Analysis are ongoing to determine if SCD-modifying therapies will impact the association between low BMD and pain. Bone biomarker studies are also pending. Further, the thoracolumbar morphometry is still undergoing radiologic review, so we can further assess how vertebral compression fractures (i) correlate with pain scores, and/or (ii) attenuate the association between low BMD and pain. Identifying and treating risk factors for low BMD may alleviate bone pain and potentially improve quality of life for all people with SCD.

Disclosures No relevant conflicts of interest to declare.

Table 1: Baseline characteristics of SCD Bone Pain Study participants (N=30)

Age (years)	
Mean (SD)	36.7 (11.44)
Sex, n (%)	
Female	21 (70)
Male	9 (30)
SCD genotype, n (%)	
HbSS/Sβ^0	20 (66.7)
HbSC	8 (26.7)
HbSβ$^+$	2 (6.6)
SCD modification, n (%)	
Hydroxyurea	16 (53.3)
Chronic RCE	7 (23.3)
L-glutamine	6 (20)
Voxelator	4 (13.3)
Crizanlizumab	3 (10)
Chronic opioids, n (%)	21 (70)
Low BMD, n (%)	12 (40)
Osteonecrosis, n (%)	11 (36.7)
BMD (g/cm^2)	
Total hip	1.001 (0.265)
Lumbar spine (L1-L4)	1.021 (0.242)
BMD Z-scores	
Total hip	-0.312 (1.710)
Lumbar spine (L1-L4)	-0.639 (2.311)

SCD Sickle cell disease; SD Standard deviation; RCE Red cell exchange transfusions; BMD Bone mineral density; Low BMD = BMD Z-score ≤ -2 at any measured site, Osteonecrosis (present in any joint)
NOTE: BMD (g/cm2) and BMD Z-scores presented as mean (SD)

Table 2: Multivariate analyses of low BMD and BMD Z-scores (hip, lumbar spine) with ASQCE-Me pain scores, adjusted for LASSO-selected covariates

Variables	Estimate	Std Error	t-value	p-value
(Intercept)	59.636	6.789	8.784	n/a
Low BMD*	-10.851	4.478	-2.423	0.0237
Vitamin D	-0.215	0.169	-1.276	0.2145
WBC	-1.253	0.534	-2.347	0.0279
Indirect bilirubin	3.099	1.407	2.204	0.0378
(Intercept)	55.456	7.802	7.107	4e10^{-8}
Hip BMD Z-score**	2.848	1.427	1.996	0.0585
Vitamin D	-0.242	0.175	-1.279	0.182
WBC	-1.068	0.587	-1.82	0.0824
Indirect bilirubin	2.828	1.461	1.935	0.0659
(Intercept)	55.643	7.293	7.629	1e10^{-8}
Lumbar BMD Z-score**	2.612	1.104	2.365	0.0268
Vitamin D	-0.249	0.167	-1.492	0.1493
WBC	-0.845	0.59	-1.433	0.1654
Indirect bilirubin	2.974	1.395	2.131	0.44

BMD Bone mineral density, ASCQ-Me Adult Quality of Life Measurement Information System, LASSO Least absolute shrinkage and selection operator, WBC White blood cell count, *categorical measure, ** continuous measure

Figure 1

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