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Bone Health in Children and Youth with Cystic Fibrosis: A Systematic Review and Meta-Analysis of Matched Cohort Studies

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Objective To assess the evidence regarding the differences in areal bone mineral density (aBMD) between children and adolescents with cystic fibrosis (CF) compared with their healthy peers, based on data from longitudinal studies.

Study design We searched MEDLINE, SPORTDiscus, the Cochrane Library, PEDro (Physiotherapy Evidence Database), and Embase databases. Observational studies addressing the change of aBMD in children with CF and healthy children and adolescents were eligible. The DerSimonian and Laird method was used to compute pooled estimates of effect sizes (ES) and 95% CIs for the change of whole body (WB), lumbar spine (LS), and femoral neck (FN) aBMD.

Results Six studies with participants with CF and 26 studies with healthy participants were included in the systematic review and meta-analysis. For the analysis in children with CF, the pooled ES for the change of WB aBMD was 0.29 (95% CI –0.15 to 0.74), for the change of LS aBMD was 0.13 (95% CI –0.16 to 0.41), and for the change of FN aBMD was 0.09 (95% CI –0.39 to 0.57). For the analysis in healthy children, the pooled ES for the change of WB aBMD was 0.37 (95% CI 0.26-0.49), for the change of LS aBMD was 0.13 (95% CI –0.16 to 0.41), and for the change of FN aBMD was 0.52 (95% CI 0.19-0.85).

Conclusions aBMD development might not differ between children and adolescents with CF receiving medical care compared with their healthy peers. Further longitudinal studies in a CF population during growth and development are required to confirm our findings. *(J Pediatr 2019;215:178-86)*.

Cystic fibrosis (CF) is the most prevalent monogenetic autosomal-recessive disorder in the white population, caused by a genetic mutation in the CF trans-membrane conductance regulator.[1] Long-term consequences include low areal bone mineral density (aBMD), osteoporosis-related fractures, and abnormal excessive convex curvature of the spine (eg, kyphosis),[2] which, in turn, may cause pain when breathing, impair physical activity levels, and reduce bone accrual.[3] The link between low aBMD and CF can be explained by multiple factors, including poor nutritional status, nutrient malabsorption, hypogonadism, physical inactivity, use of glucocorticoid therapy, and clinical status.[4-6] Moreover, bone acquisition occurs throughout childhood and adolescence, with 80%-90% of the adult skeleton acquired by late adolescence.[7] Therefore, the origins of low aBMD in patients with CF are likely to occur during childhood or adolescence.

The scientific evidence regarding bone mineralization in CF is controversial.[8-10] Some evidence indicates the prevalence of low aBMD in children and adolescents[11-13] and suggests lung function and nutritional status as important determinants of low aBMD in CF.[8,13-15] In contrast, other studies have highlighted a minimal difference in bone mass in CF (relative to normal), but this difference was more important at later life stages, such as adulthood.[16-18] This systematic review and meta-analysis was designed to synthesize the evidence regarding the differences in aBMD between children and adolescents with CF compared with their healthy peers based on data from longitudinal studies.

aBMD	Areal bone mineral density
CF	Cystic fibrosis
DXA	Dual-energy X-ray absorptiometry
ES	Effect size
FN	Femoral neck
LS	Lumbar spine
MOOSE	Meta-analysis of Observational Studies in Epidemiology statements
WB	Whole body

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L.M. is supported by Programa de Captación de Talento - UGR Fellows, from the University of Granada. The authors declare no conflicts of interest.

0022-3476/$ - see front matter.
https://doi.org/10.1016/j.jpeds.2019.07.073

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