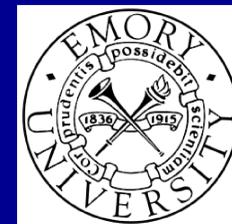


Fontan palliation in children is associated with bone deficits



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Background

Survivors with Fontan circulation suffer from chronic systemic hypoperfusion resulting in end-organ injury. Little is known about the effects of these hemodynamic perturbations on bone.

Hypothesis

Chronic Fontan circulation (>5 years after surgery) is associated with bone deficits.

Methods

Peripheral quantitative computed tomography (pQCT) was performed on 10 Fontan patients (7 males, 11.8±1.7 years) and 11 healthy controls (9 males, 12.0±1.5 years) with Tanner stage ≤ 3. Height-adjusted bone mineral density Z-scores for lumbar spine (LBMD) and total body less head (TBLH) were also measured in Fontan patients by dual energy x-ray absorptiometry (DXA). Linear regression was used to compare radius pQCT measures of bone strength index (BSI), trabecular (3% site) and cortical (33% site) volumetric BMD (vBMD), thickness, bone mineral content (BMC), cross-sectional area (CSA), polar section modulus (Zp), and strength strain index (SSI) between Fontan patients and controls, and to correlate pQCT outcomes with DXA Z-scores.

Results

Fontan patients (N=10) and controls (N=11) were similar in terms of sex, race, age, pubertal development, and anthropometrics Table 1).

Table 1. Patient characteristics

	Fontan	Controls	P-value
Male	7 (70%)	9 (82%)	0.903
Race/Ethnicity			
- American Indian	1 (10%)	0 (0%)	0.468
- Black	1 (10%)	0 (0%)	
- Hispanic/Latino	1 (10%)	2 (18%)	
- White	7 (70%)	9 (82%)	
Tanner - Pubic Hair			
- 1	4 (40%)	7 (64%)	0.556
- 2	3 (30%)	2 (18%)	
- 3	3 (30%)	2 (18%)	
Age	11.8 (1.7)	12.0 (1.5)	0.737
Height Z-Score	-0.1 (1.3)	-0.6 (1.0)	0.317
Weight Z-Score	-0.1 (0.9)	-0.6 (0.9)	0.203
BMI Z-Score	0.0 (1.0)	-0.28 (0.8)	0.464

Values presented are mean (SD) or N (%) where indicated.

- Fontan patients had lower adjusted means for trabecular vBMD, total vBMD, cortical thickness, and bone strength index (BSI).

Table 2. Linear regression results of adjusted differences in means of Fontan vs. pQCT controls in bone outcomes.

Fontan	Units	Controls	P-value
Trabecular vBMD	mg/cm ³	-28.1 (-54.8, -1.3)	0.040
Trabecular CSA	mm ²	25.0 (-37.2, 87.2)	0.431
Total vBMD	mg/cm ³	-41.0 (-78.4, -3.6)	0.032
Total CSA	mm ²	-30.4 (-99.3, 38.4)	0.387
Cortical vBMD	mg/cm ³	-10.9 (-49.8, 28.0)	0.584
Cortical CSA	mm ²	-6.0 (-15.1, 3.2)	0.204
Cortical BMC	mg/mm	-7.0 (-17.2, 3.2)	0.181
Cortical thickness	mm	-0.35 (-0.64, -0.06)	0.017
Periosteal circumference	mm	-0.3 (-2.8, 2.2)	0.821
Endosteal circumference	mm	1.9 (-0.7, 4.6)	0.153
Total BSI	mg ² /mm ⁴	-7.2 (-13.7, -0.8)	0.028
Polar Section Modulus (Zp)	mm ³	-9.3 (-51.1, 32.6)	0.664
Strength Strain Index (SSI)	mm ³	-12.6 (-47.4, 22.3)	0.480

Measures of bone density and geometry were adjusted for radius length, age, and sex, and measures of bone strength were adjusted for age and sex.

- Mean height-adjusted LBMD Z-score in Fontan patients was -0.46 ± 1.1 and TBLH Z-score was -0.63 ± 1.1.
- LBMD Z-scores were trending higher by 0.39 per 20 mg/cm³ of trabecular vBMD among Fontan patients.

Table 3. Results of a regression analysis of corrected BMD Z-scores on BMD measurements adjusting for radius length.

	Covariate	Estimate (95% CI)	P-value
cLBMD Z-score	Radius trabecular BMD (per 20 units)	0.39 (-0.006, 0.786)	0.054
cTBLH BMD Z-score	Radius Cortical BMD (per 20 units)	0.11 (-0.251, 0.466)	0.557

DXA data were available for 7 Fontan subjects.

Conclusion

Children with Fontan palliation have lower trabecular vBMD, total vBMD, cortical thickness, and bone strength index. This suggests that bone metabolism is sensitive to the Fontan physiology. Among pQCT outcomes, trabecular vBMD showed a similar trend as LBMD, underscoring a potential utility of DXA, which is more widely available than pQCT, as a monitoring tool. Further studies should evaluate the etiology and impact on fracture risk of these deficits.

Supported by the NHLBI R01HL110957, the National Center for Advancing Translational Sciences of the NIH Award Number UL1TR000114, NCATS UL1TR000114, Irvine McQuarrie Research Scholar award, and the Children's Heart Foundation.