July 22nd, 2022

CPEG Fellowship Report **Babalola, Funmbi**

Dear CPEG Committee,

Thank you for financially supporting my third-year fellowship, which allowed me to complete my Master of Science and Clinical Investigator Program at the University of Toronto. I was also able to get additional training in calcium and bone health at my fellowship program at The Hospital for Sick Children. I have successfully defended my thesis and manuscripts from my thesis are in progress. Summary of my accomplishments in my third year of fellowship are below as well as summary of my research project.

Research Abstract

Title: Bone Health in Young Adults with Type 1 Diabetes and Progressive eGFR decline

Objectives: To determine if eGFR decline in youth with type 1 diabetes (T1D) is associated with worse bone health, assessed by High Resolution Peripheral Quantitative Computed Tomography (HRpQCT) and serum bone biomarkers. Secondarily, to assess the impact of demographic and diabetes variables on bone health

Methods: Linear mixed effect model was used to generate subject specific eGFR slopes using CKiDU25 creatinine-sex adjusted eGFR measurements at 4 time points. Participants were classified as eGFR decliners if eGFR slope was ≤ -3ml/min/1.73m^2/year, corresponding to a greater eGFR decline. Measures of bone health was assessed at end of study using HRpQCT and serologic bone biomarkers: osteocalcin, procollagen-type-1-N-terminal-propeptide (P1NP), bone-specific-alkaline-phosphatase (bALP), and C-terminal-cross-linked-telopeptide (CTX). Linear regression analysis with adjustment for covariates was performed.

Results: There were 99 participants, of which 45% were male, assessed over an average of 7.4 ± 1 years, beginning at 14 ±1.7 to 21.3 ± 2.1 years. Mean eGFR over time was 103.7 ± 4.8 ml/min/1.73m^2 with median eGFR slope of -2.8 (-4.7, -0.7) ml/min/1.73m^2/year. 44% of study participants were eGFR decliners. Median diabetes duration was 13.7 (11.8, 16.0) years with cumulative average hemoglobin A1C of 8.25 (±0.95)%. 26% of study participants had optimal 25 hydroxyvitamin D ≥75nmol/L.

eGFR decliners had 5% higher tibia cortical porosity diameter than non-decliners in the linear regression adjusted model (p = 0.035). None of the other HRpQCT parameters or bone biomarkers were statistically significant in the adjusted model.

Increase in 25 hydroxy-vitamin D level was associated with decrease in tibia trabecular separation (p=0.01). As diabetes duration increased, trabecular separation increased (p = 0.004) and trabecular number decreased (p = 0.01) . As A1C increased, P1NP decreased (p = 0.008). Increasing BMI was associated with decrease in osteocalcin (p = 0.009) Males had higher values

than females in most HRpQCT parameters except for trabecular separation and cortical volumetric bone mineral density.

Conclusion: This study presents a novel finding of increased cortical porosity diameter in patients with T1D and progressive eGFR decline. This is an early microarchitectural change suggestive of worse bone health. It highlights a group for potential intervention to prevent complication of worsened bone health later on in adulthood. Currently, studies show increased skeletal fragility in T1D and further work on early signs of kidney disease could potentially help better classify at risk patients for skeletal fragility.

Higher BMI and A1C were associated with decreased bone formation, emphasizing the importance of healthy BMI and optimal glycemic control in patients with T1D. There was an association between 25 hydroxy-vitamin D and trabecular separation, highlighting the importance of vitamin D in bone health in patients with T1D

Presentations

1. Canadian Pediatric Endocrine Group Conference, February 2022 - oral
2. U of T IMS Research Day, May 2022 - poster
3. SickKids Research Day, May 2022 - poster
4. American Diabetes Association, June 2022 - poster
5. International Conference of Children's Bone Health, June 2022 - poster

Awards

1. Early Investigator Award: Awarded to high-ranking abstracts at the International Conference of Bone Health
2. International Society of Pediatric and Adolescent Diabetes Science School: Prestigious opportunity awarded to select applicants
3. John Bailey Award: CPEG

Publications

Babalola F, Ng Dominic, Bulic , Curtis Jacqueline. Successful treatment of severe hypertriglyceridemia with icosapent ethyl in a case of congenital generalized lipodystrophy type 4. Journal of Pediatric Endocrinology and Metabolism. 2022;aop

Babalola F, Miller M, Ens A, Stein R, Gallego P, Clarson C. Frequency of diabetes team contacts in children and adolescents using insulin pumps. *Clinical Diabetology*. 2022. 11(1): 6 – 10.