

Serum biomarkers, but not Dual Energy X-ray Absorptiometry, predict cortical bone mineral density in children and young adults with CKD

Dr Alexander D. Lalayiannis¹, Dr Nicola J. Crabtree², Prof Charles J. Ferro³, Dr Varvara Askiti⁴, Dr Andromache Mitsioni⁴, Dr Lorenzo Biassoni¹, Dr Amrit Kaur⁵, Dr Manish D. Sinha⁶, Prof David C. Wheeler⁷, Dr Neill D. Duncan⁸, Dr Joyce Popoola⁹, Dr David V. Milford², Prof Mary Fewtrell¹, Dr Rukshana Shroff¹

¹Great Ormond St Hospital for Children NHS Foundation Trust, and University College London Institute of Child Health, London, United Kingdom, ²Birmingham Women's and Children's NHS Foundation Trust, Birmingham, United Kingdom, ³University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, ⁴"P. & A. Kyriakou" Children's Hospital, Athens, Greece, ⁵Manchester University NHS Foundation Trust, Manchester, United Kingdom, ⁶Evelina Children's Hospital, Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom, ⁷Royal Free Hospital NHS Foundation Trust & Department of Renal Medicine, University College London, London, United Kingdom, ⁸Imperial College Renal and Transplant Centre, Hammersmith Hospital, London, United Kingdom, ⁹Department of Nephrology and Transplantation, St. George's University Hospital NHS Foundation Trust, London, United Kingdom

Introduction

Currently available biomarkers and Dual-energy X-ray Absorptiometry(DXA) are thought to be poor predictors of bone mineral density(BMD). The 2017 KDIGO guidelines on chronic kidney disease mineral bone disorder(CKD-MBD) propose using DXA if it will affect patient management or if the patient is at risk of fractures. This recommendation is based on evidence from older people with CKD, and may not be relevant in young patients.

We set out to determine the clinical utility of DXA and routine clinical biomarkers in the young CKD population, by comparing them with tibial cortical BMD measured by peripheral Quantitative Computed Tomography(pQCT). pQCT clearly defines cortical and trabecular bone compartments, and tibial cortical BMD Z-score predicts future fracture risk in CKD[1].

Methods

We performed a prospective multi-centre cross-sectional study: 77 participants on dialysis and 26 in CKD4-5(n=103 total) were compared with 62 age-matched healthy volunteers. Patients under 30 years of age were studied as bone mineral accretion may continue up to 30 years of age when peak bone mass is achieved. Participants underwent hip and lumbar spine(LS) DXA [for areal BMD (aBMD)] , tibial pQCT(for volumetric BMD) and measurement of routine serum biomarkers. All pQCT and DXA measures were expressed as Z-scores adjusted for age, sex, race and height or growth as appropriate. Tibial cortical BMD Z-scores was used as the gold standard to evaluate the predictive value of other measures.

Results

CKD-MBD related morbidity, such as bone pain that hindered activities of daily living was present in 58% of participants. 10% suffered from at least one previous low-trauma fracture.

Hip Z-scores were significantly lower in dialysis compared to CKD or healthy participants (p=0.01 & p<0.001). DXA LS Z-scores were higher in CKD compared to the dialysis population, with a corresponding higher tibial trabecular BMD Z-score on pQCT (p=0.006 & p=0.02). pQCT tibial cortical BMD and cortical mineral content Z-scores were significantly lower in dialysis compared to CKD patients (p=0.01 & p=0.05 respectively)(Figures 1a and b).

Hip Z-scores and LS aBMD Z-scores did not correlate with any biomarkers or tibial cortical BMD, nor with each other(R²= 0.028, p=0.07).

Serum calcium showed a positive correlation with tibial trabecular BMD and cortical BMD Z-scores ($r=0.32$, $p=0.001$ and $r=0.33$, $p=0.001$ respectively). Tibial cortical BMD Z-scores were negatively associated with parathyroid hormone (PTH)($r=-0.44$, $p<0.001$) and alkaline phosphatase (ALP)($r=-0.22$, $p=0.03$). On multivariable linear regression analysis the significant and independent predictors of tibial cortical BMD Z-scores were PTH ($\beta-0.39$, $p<0.001$), ALP ($\beta-0.35$, $p<0.001$) and serum calcium ($\beta 0.20$, $p=0.015$), which together predicted 52% of variability in tibial cortical pQCT. DXA imaging did not improve this model.

Conclusions

Routinely used biomarkers, calcium, ALP and PTH, when used together are moderate predictors of cortical BMD. No associations were seen with hip or lumbar spine DXA, suggesting that DXA is not a clinically useful tool in this population and should not be performed routinely in children and young adults with CKD4-5 and on dialysis. The predictive value of biomarkers and imaging in determining key patient-level outcomes such as fractures requires further study.