Post–Renal Transplantation Bone Health in Children Evaluated by Means of Quantitative Ultrasound and Densitometry

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ABSTRACT

Background. Patients with end-stage renal disease develop bone mineral disease, which is not always resolved after a successful renal transplantation; moreover, some of the immunosuppressants used to prevent graft rejection may affect bone health. The aim of this study was to evaluate bone health in post–renal transplantation children with the use of quantitative ultrasound (QUS) and dual-energy X-ray absorptiometry (DXA).

Methods. A descriptive study was performed in children >3 months after renal transplantation and with stable function of graft. Radial QUS and DXA (lumbar spine and total body less head (TBLH) were performed on the same day.

Results. A total of 35 patients were included. Mean age was 13.9 ± 3.9 years. Ten subjects had total bone density score <2 (28.5%), 4 a lumbar spine (L1-L4) Z-score of <2 (11.4%) as well as TBLH <2, and 6 subjects had a radial QUS Z-score of <2 (17.1%), and only 2 of them had concomitant Z-score <2 with the use of DXA. There was a positive non-significant correlation between TBLH and radial QUS Z-scores (Pearson $r = 0.317$; $P = .016$) and a positive significant correlation of DXA lumbar spine and radial QUS Z-scores (Pearson $r = 0.452$; $P = .014$).

Conclusions. Despite a good correlation between TBLH and QUS Z-scores, there are subjects that can be considered normal by QUS and have osteopenia by TBLH DXA and vice versa; this could be due to the different bone areas evaluated.

MINERAL BONE DISORDER is common in patients with renal disease [1]. Renal transplantation is considered to be the best therapeutic option for children with end-stage renal disease; nevertheless, renal transplant patients with normal graft function persist with bone disease attributed to immunosuppressive drugs (steroids and calcineurin inhibitors). Children with solid organ transplantation are at higher risk of bone fractures [2].

Mineral bone status can be assessed in children and adolescents by means of dual-energy X-ray absorptiometry (DXA), which provides information on bone mineral content and bone mineral density. The skeletal sites recommended in children are total body less head (TBLH) and lumbar spine (L1-L4), and there are normative databases available considering sex- and age-specific standard deviation scores (Z-scores) [3]. This technique is highly reproducible and represents a low radiation exposure. The preferred method to evaluate bone health in chronic kidney disease children is transiliac bone biopsy with the use of tetracycline labeling, which provides information on bone properties in bone formation, and bone resorption. Bone histomorphometry has a wide spectrum of bone disease (low, normal, and high

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Table 1. Demographics of 35 Renal Transplant Children

Characteristic	Value
Age, y	14.1 ± 3.5
Sex	
Male	17 (48.6%)
Female	18 (51.4%)
Z-score, height	−1.93 ± 1.23
Source of graft	
Living donor	15 (42.9%)
Deceased donor	20 (57.1%)
Cause of renal disease	
GMN	7 (20%)
CAKUT	4 (11.4%)
Other	3 (8.6%)
Unknown	21 (60%)
Time on dialysis before transplantation, mo	15 (7, 33)
Immunosuppression	
Tacrolimus	33 (94.3%)
Cyclosporine	2 (5.7%)
Mofetil mycophenolate	35 (100%)
Tacrolimus trough levels, ng/mL	8 (6.7–9.7)
Time after renal transplant, mo	4.8 ± 2.6

Note. Values are presented as mean ± SD, n (%), or median (interquartile range).
Abbreviations: GMN, glomerulonephritis; CAKUT, congenital anomalies of kidney and urinary tract.

turnover), and the disease has different effects on trabecular and cortical bone [1]. However, bone biopsy is an invasive procedure rarely performed in a routine follow-up. Studies in dialysis children have shown that DXA do not correlate with bone biopsy findings [4,5], and DXA is recommended to follow-up renal transplant recipients [6–8].

Quantitative ultrasound (QUS) is a radiation-free, safe, and easy-to-use technique to evaluate bone mineral status in children and can be applied to different skeletal sites (heel, tibia, radius, proximal phalange) [9]. It has been shown to be useful to predict bone fractures in adults [10], and there are studies that have shown good correlation with DXA [11].

The aim of the present study was to evaluate bone health in post–renal transplantation children with the use of QUS and DXA densitometry.

PATIENTS AND METHODS

The study was approved by the Institutional Review Board and Ethics Committee and conducted according with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent/assent was obtained from every participant.

Patients aged 5–17 years, recipients of a 1st renal graft, and >3 months with stable kidney function were invited to participate.

Anthropometry

Height and weight were measured with patients barefoot and dressed in underwear only. Standing height was measured to the nearest 0.1 mm with the use of a stadiometer. Weight adjusted to the nearest 0.1 kg was measured with an electric scale (ADE model M201610; Hamburg Germany). Z-Scores by age and sex were obtained from the World Health Organization growth charts.

Imaging Studies

Bone mineral densitometry (TBLH and lumbar spine) was measured with the use of a Lunar iDXA (General Electric Healthcare) and non–dominant hand radial QUS.

Imunosuppression

Our institution's transplant protocol includes induction with basiliximab, steroids (3 methylprednisolone pulses and then prednisone tapered), mofetil mycophenolate, and tacrolimus.

Clinical examination, QUS, and DXA were performed on the same day. A serum sample for biochemical exam was obtained for serum creatinine, calcium, phosphate, magnesium, alkaline phosphatase, serum albumin, parathyroid hormone (PTH), and serum fibroblast growth factor (FGF) 23. Glomerular filtration rate was estimated by means of the Schwartz bedside formula [12].

Statistical Analysis

Descriptive statistics are reported as mean ± SD or median (interquartile range) for continuous variables and as percentages for binary/categoric variables. Correlation between DXA (TBLH and lumbar spine) and QUS Z-scores were determined by means of Pearson correlation, with $P < .05$ (2 sided) considered to be statistically significant. All analysis were performed with the use of Graphpad Prism for Mac OS X, version 5.0.

RESULTS

We included 35 subjects. Patient demographics are presented in Table 1: mean age 14.1 ± 3.5 years, 18 girls (51.4%), 20 with a kidney from a deceased donor (57.1%), and cause of end-stage renal disease unknown in 21 (60%) and glomerulonephritis in 7 (20%).

Biochemical variables, radial QUS Z-score, and TBLH and lumbar spine DXA Z-score are presented in Table 2. Ten patients had DXA TBLH Z-score <2 (28.6%), 4 of

Table 2. Imaging Studies and Biochemical Results

Characteristic	Value
DXA, lumbar spine	
Z-score <2	4 (11.4%)
Mean Z-score	−1.30 ± 1.48
DXA, TBLH	
Z-score <2 (*n*, %)	10 (28.6%)
Mean Z-score	−1.30 ± 0.99
Radial QUS	
Z-score <2	6 (17.1%)
Mean Z-score	0.014 ± 2.46
Serum creatinine, mg/dL	0.9 (0.7–1.3)
Glomerular filtration rate, mL/min/1.73 m^2	62.16 ± 17.50
Parathyroid hormone, pg/mL	77 (44–106)
FGF23, pg/mL	224 (17.4–1449)
Calcium,* mg/dL	9.45 ± 0.61
Phosphate, mg/dL	4.49 ± 0.94
Alkaline phosphatase, UI/L	257 (153–304)
Magnesium, mg/dL	1.71 ± 0.26

Note. Values are presented as n (%), mean ± SD, or median (interquartile range).
Abbreviations: DXA, dual-energy X-ray absorptiometry; TBLH, total body less head; QUS, quantitative ultrasound; FGF, fibroblast growth factor.
*Calcium was corrected by albumin.