I – J Am Soc Nephrol. 2015 Jul 2: ASN.2015020152.

Fracture Burden and Risk Factors in Childhood CKD: Results from the CKiD Cohort Study.

Denburg MR, Kumar J, Jemielita T, Brooks ER, Skversky A, Portale AA, Salusky IB, Warady BA, Furth SL, Leonard MB

Childhood chronic kidney disease (CKD) poses multiple threats to bone accrual; however, the associated fracture risk is not well characterized. This prospective cohort study included 537 CKD in Children (CKiD) participants. Fracture histories were obtained at baseline, at years 1, 3, and 5 through November 1, 2009, and annually thereafter. We used Cox regression analysis of first incident fracture to evaluate potential correlates of fracture risk. At enrollment, median age was 11 years, and 16% of patients reported a prior fracture. Over a median of 3.9 years, 43 males and 24 females sustained incident fractures, corresponding to 395 (95% confidence interval [95% CI], 293-533) and 323 (95% CI, 216-481) fractures per 10,000 person-years, respectively. These rates were 2- to 3-fold higher than published general population rates. The only gender difference in fracture risk was a 2.6-fold higher risk in males aged ≥15 years (570/10,000 person-years, adjusted P=0.04). In multivariable analysis, advanced pubertal stage, greater height Z-score, difficulty walking, and higher average log-transformed parathyroid hormone level were independently associated with greater fracture risk (all P≤0.04). Phosphate binder treatment (predominantly calcium-based) was associated with lower fracture risk (hazard ratio, 0.37; 95% CI, 0.15-0.91; P=0.03). Participation in more than one team sport was associated with higher risk (hazard ratio, 4.87; 95% CI, 2.21-10.75; P<0.001). In conclusion, children with CKD have a high burden of fracture. Regarding modifiable factors, higher average parathyroid hormone level was associated with greater risk of fracture, whereas phosphate binder use was protective in this cohort.

II - Am J Kidney Dis. 2015 Jul 21. pii: S0272-6386(15)00922-1. doi: 10.1053/j.ajkd.2015.06.015. [Epub ahead of print]

Hyperuricemia and Progression of CKD in Children and Adolescents: The Chronic Kidney Disease in Children (CKiD) Cohort Study.

Rodenbach KE, Schneider MF, Furth SL, Moxey-Mims MM, Mitsnefes MM, Weaver DJ, Warady BA, Schwartz GJ.

Abstract

BACKGROUND

Hyperuricemia is associated with essential hypertension in children. No previous studies have evaluated the effect of hyperuricemia on progression of chronic kidney disease (CKD) in children.

STUDY DESIGN

Prospective observational cohort study.

SETTING & PARTICIPANTS

Children and adolescents (n=678 cross-sectional; n=627 longitudinal) with a median age of 12.3 (IQR, 8.6-15.6) years enrolled at 52 North American sites of the CKiD (CKD in Children) Study.

PREDICTOR

Serum uric acid level (<5.5, 5.5-7.5, and >7.5mg/dL).

OUTCOMES

Composite end point of either >30% decline in glomerular filtration rate (GFR) or initiation of renal replacement therapy.

MEASUREMENTS

Age, sex, race, blood pressure status, GFR, CKD cause, urine protein-creatinine ratio (<0.5, 0.5-<2.0, and ≥2.0mg/mg), age- and sex-specific body mass index > 95th percentile, use of diuretics, and serum uric acid level.

RESULTS

Older age, male sex, lower GFR, and body mass index > 95th percentile were associated with higher uric acid levels. 162, 294, and 171 participants had initial uric acid levels < 5.5, 5.5 to 7.5, or >7.5 mg/dL, respectively. We observed 225 instances of the composite end point over 5 years. In a multivariable parametric time-to-event analysis, compared with participants with initial uric acid levels < 5.5mg/dL, those with uric acid levels of 5.5 to 7.5 or >7.5mg/dL had 17% shorter (relative time, 0.83; 95% CI, 0.62-1.11) or 38% shorter (relative time, 0.62; 95% CI, 0.45-0.85) times to event, respectively. Hypertension, lower GFR, glomerular CKD cause, and elevated urine protein-creatinine ratio were also associated with faster times to the composite end point.

LIMITATIONS

The study lacked sufficient data to examine how use of specific medications might influence serum uric acid levels and CKD progression.

CONCLUSIONS

Hyperuricemia is a previously undescribed independent risk factor for faster progression of CKD in children and adolescents. It is possible that treatment of children and adolescents with CKD with urate-lowering therapy could slow disease progression.

Comments

Two recent papers from the North-American CKiD cohort that raise questions that should be evaluated prospectively in clinical trials in the future.

Briefly, the first paper confirms that the fracture rate in pediatric CKD is 2- to 3-fold higher than in the general population. Advanced pubertal stage, greater height Z-score, difficulty walking, and higher

PTH level were found to be independently associated with greater fracture risk. The use of phosphate binders (predominantly calcium-based) was associated with a lower fracture risk, thus questioning which type of phosphate binder (calcium-based versus non-calcium based) should be used in children with growing skeletons. Future clinical trials may focus on this very important issue for CKD-MBD management.

The second paper describes hyperuricemia as an independent risk factor for faster progression of pediatric CKD. Even though it would have been interesting to compare uric acid levels to FGF23 levels (because of the direct associations of the two variables found in previous cohorts on one hand, and because of the well-known effects of FGF23 on progression of renal disease on the other hand), this study raises the question of whether (or not) treating pediatric CKD patients with hyperuricemia with allopurinol is beneficial. Future clinical trials should also focus on this important issue.

III - **Renal transplantation**:

Deonna R. Moore, David Serur, Dianne LaPointe Rudow, James R. Rodrigue, Rebecca Hays and Matthew Cooper: Living Donor Kidney Transplantation: Improving Efficiencies in Live Kidney Donor Evaluation– Recommendations from a Consensus Conference Clin J Am Soc Nephrol 10: 1678–1686, 2015.

(http://cjasn.asnjournals.org/content/10/9/1678.long)

Short comment:

Living donor is a common clinical practice for most renal transplant Centers. The American Society of Transplantation's Live Donor Community of Practice is a group of clinicians with expertise in living kidney donation (LKD) formed in 2012 to advocate, support, and advance knowledge in the care of the live organ donor.

A consensus conference was held on June 5–6, 2014, in Rosemont, Illinois, and was supported by 11 transplant, nephrology, and patient services organizations. Their conclusions are published in six articles in the September issue of the clinical Journal of the American society of Nephrology.

This article reviews the process of living donors evaluation, suggesting how to proceed step by step and helps the referring nephrologist to improve efficiencies in the process of donor education and evaluation.

It also includes a list of required specific evaluation and assessments for donors .

Reasons for non donation are discussed.

Abstract

The education, evaluation, and support of living donors before, during, and after donation have historically been considered the roles and responsibilities of transplant programs. Although intended to protect donors, ensure true informed consent, and prevent coercion, this structure often leaves referring nephrologists unclear about the donor process and uncertain regarding the ultimate outcome

of potential donors for their patients. The aim of this article is to help the referring nephrologist understand the donor referral and evaluation process, help the referring nephrologist understand the responsibilities of the transplant program, and offer suggestions about how the referring nephrologist can help to improve efficiencies in the process of donor education and evaluate on. A partnership between referring nephrologists and transplant programs is an important step in advancing living kidney donation. The referring nephrologists are the frontline providers and are in a unique position to offer education about living donation and improve efficiencies in the process. Understanding the donor referral and evaluation process, the responsibilities of the transplant program, and the potential role referring nephrologists can play in the process is critical to establishing such a partnership. Clin J Am Soc Nephrol 10: 1678–1686, 2015. doi: 10.2215/CJN.01040115