Renal Volume in Children with ADPKD: Size Matters

Arlene B. Chapman* and Lisa M. Guay-Woodford†

*Renal Division, Emory University School of Medicine, Atlanta, Georgia; and †Department of Genetics, University of Alabama at Birmingham, Birmingham, Alabama

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Autosomal dominant polycystic kidney disease (ADPKD) is characterized by a relatively slow increase in kidney size as a result of cyst growth and expansion (1,2). Initiated *in utero*, this process continues over decades before the loss of renal function. Recent data from the Consortium for Radiologic Imaging Studies in Polycystic Kidney Disease (CRISP) study indicate that kidney growth is a critical predictor of progression to renal failure in ADPKD, playing a more important role than hypertension, proteinuria, age, or gender (3). Modeling experiments using prospective clinical data from the CRISP cohort have suggested that very high rates of kidney growth must occur during childhood to account for the kidney volumes observed in adults (4).

Although CRISP and other studies have addressed the issue of early renal disease progression in adults with ADPKD, there are few comparable studies of children. In this issue of *CJASN*, Cadnapaphornchai *et al.* (5) report a 5-yr randomized clinical trial that assessed early disease progression (measured by renal volume) and the effect of BP control with angiotensin-converting enzyme inhibition (ACEI) in 85 children and young adults with ADPKD.

Participants were stratified into three groups: Hypertension (BP >95th percentile), borderline hypertension (BP 75 to 95th percentile), and severe ADPKD (SPKD; BP <75th percentile with >10 renal cysts). In the group with hypertension, participants were randomly assigned to BP targets of either ≤90th or ≤50th, whereas those in the groups with borderline hypertension and SPKD were randomly assigned to ACEI treatment or no treatment. The primary outcome variable was renal volume assessed by ultrasound imaging. Secondary outcome variables included left ventricular mass index (LVMI) and microalbuminuria.

Although the authors did not follow the consensus guidelines established by the 2004 Task Force on BP stratification in children (6), it must be noted that this study was initiated before 2004 and the definition of "prehypertension" in children (BP 90 to 95th percentile) was too narrow for meaningful statistical analysis. Therefore, children with BP between the 75th and 95th percentiles were classified as having borderline hypertension, a designation supported by increased left ventricular mass as compared with children with BP <75th percentile (7).

This study provides the most comprehensive assessment of early kidney disease progression in children with ADPKD, taking into account the impact of hypertension and ACEI treatment. The data demonstrate that children with hypertension experience an aggressive increase in renal volume as compared with their counterparts with normotension (estimated >14 *versus* <9% per year). It is interesting that the rate of increase in both groups exceeded the rate of renal volume progression observed in CRISP participants with hypertension and normal renal function (6.2% per yr) (3). Although no significant benefits on renal volume were observed with renin-angiotensin-aldosterone system inhibition, the proportion of participants who achieved their BP targets was relatively low and the study groups were small. It is interesting that during the course of the study, children with hypertension experienced a significant decline in renal function. Given the study design, the authors cannot distinguish whether this decline is a primary hypertension-related event or reflects a secondary decrease in hyperfiltration as a result of ACEI. Nonetheless, once hypertension was established, ACEI alone did not affect the deterioration in renal function or increase in LVMI. In contrast, ACEI treatment in children with borderline hypertension seemed to attenuate LVMI increase and stabilize renal function. In addition, ACEI reduced urinary albumin excretion in children with SPKD. Taken together, the data suggest that ACEI treatment may particularly benefit children with BP in the high-normal range (75 to 95th percentiles).

This study validates observations previously reported in children with ADPKD. Specifically, children with ADPKD and hypertension have larger kidney volumes as compared with their counterparts with normotension (8). There is a significant association between LVMI and renal volume in children with hypertension (7). There was a linear relationship between age and renal volume in children with ADPKD and normotension, whereas children with hypertension exhibited a significant curvilinear relationship, suggesting that these children are at significant risk for deteriorating renal function early in adulthood.

In summary, despite minor design issues, the study reported by Cadnapaphornchai *et al.* demonstrates that children with ADPKD and with BP >75th percentile are at particular risk for deterioration in their renal and cardiovascular status. These data identify a subgroup of children who have ADPKD and for whom targeted therapeutic intervention (*e.g.*, with vasopressin receptor antagonists) may be warranted in childhood.

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Correspondence: Dr. Lisa M. Guay-Woodford, University of Alabama at Birmingham, Kaul Building 740, 720 South 20th Street, Birmingham, Alabama 35294. Phone: 205-934-7308; Fax: 205-975-5689; E-mail: lgw@uab.edu

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Disclosures

None.

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See related article, "Prospective Change in Renal Volume and Function in Children with ADPKD," on pages 820–829.