A comparison of ultrasound and magnetic resonance imaging shows that kidney length predicts chronic kidney disease in autosomal dominant polycystic kidney disease

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Autosomal dominant polycystic kidney disease (ADPKD) is marked by gradual renal cyst and kidney enlargement and ultimately renal failure. Magnetic resonance–based, height-adjusted total kidney volume (htTKV) over 600 cc/m predicts the development of CKD stage 3 within 8 years in the Consortium for Radiologic Imaging in Polycystic Kidney Disease cohort. Here we compared simultaneous ultrasound and magnetic resonance imaging to determine whether ultrasound and kidney length (KL) predict future CKD stage 3 over longer periods of follow-up. A total of 241 ADPKD patients, 15–46 years, with creatinine clearance of 70 ml/min and above had iothalamate clearance, magnetic resonance, and ultrasound evaluations. Participants underwent an average of five repeat clearance measurements over a mean follow-up of 9.3 years. Ultrasound and magnetic resonance-based TKV and KL were compared using Bland–Altman plots and intraclass correlations. Each measure was tested to predict future CKD stage 3. Relatively strong intraclass correlations between ultrasound and magnetic resonance were found for both htTKV and KL (0.81 and 0.85, respectively). Ultrasound and magnetic resonance-based htTKV and KL predicted future CKD stage 3 similarly (AUC of 0.87, 0.88, 0.87, and 0.88, respectively). An ultrasound kidney length over 16.5 cm and htTKV over 650 ml/min had the best cut point for predicting the development of CKD stage 3. Thus, kidney length alone is sufficient to stratify the risk of progression to renal insufficiency early in ADPKD using either ultrasound or magnetic resonance imaging.

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Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary kidney disorder and the fourth leading cause of renal failure in the United States, accounting for 4.8% of the end-stage renal disease population.[1] In ADPKD, cysts develop and subsequently enlarge, resulting in increased kidney size decades before decline in kidney function, with end-stage renal disease typically occurring in the sixth decade of life.[2] Recently, renal cyst burden measured as total kidney volume (TKV) determined by magnetic resonance imaging (MR) has been shown to be accurate, reproducible, and able to detect small changes in TKV over a short period of time.[3] TKV independently and strongly predicts the future development of chronic kidney disease (CKD) stage 3 within 8 years in ADPKD with a threshold of 1047 ml or 600 ml/min when corrected for height (htTKV).[3] These data have enabled the design and implementation of several randomized clinical trials in ADPKD,[4] and large patient registries show that TKV in addition to age and kidney function confidently predicts a 30% decline in kidney function, doubling of serum creatinine concentration, and progression to end-stage renal disease.[3] This increasing body of evidence has led to TKV being reviewed by the Food and Drug Administration as an enrichment biomarker for inclusion in clinical trials of ADPKD.[4]

Although highly accurate and reproducible, TKV measurements by MR are time-consuming, expensive, and not available to all patients. MR relies on specific image acquisition parameters, patient adherence, and relatively manual and time-intensive image analyses performed by trained personnel. Alternative approaches to estimate TKV from MR images have been developed. In one approach, a representative mid-slice surface area is multiplied by the slice thickness and the number of slices required to image the entire kidney.[5] Another approach uses the ellipsoid formula based on maximum coronal or sagittal dimensions for kidney length and axial dimensions for width and depth.[6] This approach has been used successfully with ultrasound (US) to follow TKV in

Table 1 | Baseline characteristics of CRISP participants

Variable	Mean ± s.d.	Women, *N* = 145	Men, *N* = 96
Age (years)	33.8 ± 8.9	34.0 ± 9.0	33.5 ± 8.8
Weight (kg)	77.0 ± 18.4	69.7 ± 15.8	88.1 ± 16.6
BMI (m^2)	25.9 ± 5.2	25.5 ± 5.6	26.5 ± 4.7
MR htTKV (cc/m)	637.5 ± 371.8 (*N* = 231)	632.7 ± 360.9 (*N* = 138)	644 ± 389.4 (*N* = 93)
US htTKV (cc/m)	719.6 ± 506.1 (*N* = 231)	694.0 ± 496.3 (*N* = 139)	758.2 ± 520.8 (*N* = 92)
MR TKV (ml)	1093.9 ± 672.0 (*N* = 229)	1031.7 ± 620.9 (*N* = 137)	1186.6 ± 735.5 (*N* = 92)
US TKV (ml)	1247.4 ± 896.7 (*N* = 231)	1151.8 ± 836.0 (*N* = 139)	1391.9 ± 968.2 (*N* = 92)
L US KL (cm)	16.8 ± 3.9 (*N* = 232)	16.4 ± 3.8 (*N* = 139)	17.3 ± 3.9 (*N* = 93)
L MR KL (cm)	16.3 ± 3.4 (*N* = 232)	16.1 ± 3.5 (*N* = 139)	16.6 ± 3.3 (*N* = 93)
R US KL (cm)	16.2 ± 3.9 (*N* = 232)	15.9 ± 3.8 (*N* = 139)	16.5 ± 4.0 (*N* = 93)
R MR KL (cm)	15.8 ± 3.2 (*N* = 232)	15.7 ± 3.3 (*N* = 139)	15.9 ± 3.1 (*N* = 93)
SBP (mm Hg)	125.1 ± 13.6	122.7 ± 14.0	128.5 ± 12.3
DBP (mm Hg)	83.4 ± 10.7	83.2 ± 11.0	83.6 ± 10.4
MAP (mm Hg)	98.2 ± 10.9	97.4 ± 11.5	99.4 ± 9.7
Serum creatinine (mg/dl)	1.0 ± 0.2	0.9 ± 0.2	1.1 ± 0.2
GFR (ml/mm per 1.73 m^2)	98.2 ± 24.9	99.8 ± 26.6	95.8 ± 22.1
Sodium excretion (mEq per day)	185.5 ± 87.2	162.0 ± 74.8	220.9 ± 92.8
Potassium excretion (mEq per day)	56.5 ± 24.7	51.1 ± 21.3	64.7 ± 27.3
Albumin excretion (mg per day)	42.4 ± 60.9	39.4 ± 48.2	47.0 ± 76.2
Total cholesterol (mg/dl)	172.9 ± 37.0	169.2 ± 34.1	178.6 ± 40.6
HDL (mg/dl)	49.2 ± 22.6	51.8 ± 12.5	45.3 ± 31.96
LDL (mg/dl)	102.4 ± 34.3	97.6 ± 28.9	109.8 ± 40.2
Triglycerides (mg/dl)	120.2 ± 95.0	102.4 ± 63.0	147.5 ± 125.0

Abbreviations: BMI, body mass index; CRISP, Consortium for Radiologic Imaging in Polycystic Kidney Disease; DBP, diastolic blood pressure; GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; htTKV, height-adjusted total kidney volume; KL, kidney length; L, left; MAP, mean arterial pressure; MR, magnetic resonance; R, right; SBP, systolic blood pressure; US, ultrasound.

patients over extended periods (often decades) of time and associates with complications in ADPKD, such as hypertension and renal disease progression.[7] However, the accuracy and precision of US are insufficiently precise to support its use to measure TKV in interventional clinical trials. Kidney length can estimate TKV[5] and is easily obtained by US or MR. US is readily available in all medical centers, is the most commonly used imaging modality worldwide for diagnosing ADPKD, and is advantageous because of its relatively low cost and lack of radiation exposure. Estimation of TKV from kidney length reduces imaging and analysis time, as well as cost, but it is unknown how well kidney length performs in predicting the future development of CKD in ADPKD and what the impact of the imaging modality chosen (US vs. MRI) has on this prediction model.

In the Consortium for Radiologic Imaging in Polycystic Kidney Disease (CRISP) cohort, US and MR measurements were made at the baseline visit and the first year of follow-up. As anticipated, MR was more accurate and reproducible compared with US.[6] Although US accurately approximated TKV in individuals with relatively small kidneys, the agreement between US and TKV declined as kidney size increased with US systematically overestimating TKV.[6] Given the greater variability of US-based TKV measurements and the reduced precision in assessing kidney cyst burden, US was deemed inferior for the purposes of imaging biomarker development and was discontinued for the rest of the CRISP follow-up.

To assess whether US-based measurements of TKV or kidney length reliably predict future renal insufficiency in ADPKD, we compared the US and MR imaging data collected simultaneously during the baseline visit in CRISP participants, similar to previous studies evaluating htTKV measurements by MR.[3] We compared MR and US kidney length and determined the accuracy of MR- and US-based htTKV and kidney length to predict future CKD stage 3 measured by iothalamate clearance in ADPKD over 13 years of follow-up.

RESULTS

The mean follow-up (i.e. time from baseline to last measured iothalamate clearance) was 9.3 years (s.d. 3.3 years) with a median follow-up of 10.8 years. The middle 50% of follow-up times was 8.2 to 11.3 years. A total of 202 (83.8%) and 182 (75.5%) had an iothalamate clearance measured at a minimum of 6 and 8 years after baseline, respectively. Only 23 (9.5%) did not have a measurement after 3 years. The mean number of visits per person was 6.0 (s.d. = 1.6) with a median of seven visits and middle 50% of five to seven visits. Only 14 people (5.8%) had three or fewer visits.

Baseline distributions are described in Table 1; 88% were white, 60% were women, and 10% were black. Average baseline htTKV by MR was 637 ml (s.d. ± 371 ml). Average kidney length measured by US and MR for the left kidney was 16.8 ± 3.9 and 16.3 ± 3.5 cm and the right kidney was 16.2 ± 3.9 and 15.8 ± 3.2 cm, respectively. Bland–Altman plots demonstrated high levels of agreement between US and MR kidney length (Figure 1a–d) as did the scatter plots (Figure 2a and b). The bias or mean paired difference (± s.d.) of US–MR measurement was 44.2 ±127.6 ml for right and 44.9 ± 147.4 ml for left kidney htTKV and 0.39 ± 2.08 cm for right and