Kidney International, Vol. 64 (2003), pp. 2214–2221

Magnetic resonance measurements of renal blood flow as a marker of disease severity in autosomal-dominant polycystic kidney disease[1]

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Magnetic resonance measurements of renal blood flow as a marker of disease severity in autosomal-dominant polycystic kidney disease.

Background. Autosomal-dominant polycystic kidney disease (ADPKD) is an inherited disorder characterized by renal cyst growth, early development of hypertension, and late occurrence of renal insufficiency. Despite evidence for the importance of nephroangiosclerosis in the progression of renal insufficiency in ADPKD, evaluation of renal blood flow (RBF) as a surrogate marker of disease severity has received little attention.

Methods. Flow phantoms and repeat RBF measurements assessed accuracy and reproducibility. One hundred twenty-seven ADPKD subjects with creatinine clearances >70 mL/min underwent measurements of RBF, total, and cyst renal volumes, and % cyst volumes by magnetic resonance (MR) and of glomerular filtration rate (GFR). Renal vascular resistance (RVR) was calculated. MR blood flow sequences utilized a two-dimensional cine phase-contrast breath-hold pulse sequence perpendicular to the renal arteries. Flow rates were calculated utilizing FLOW software. Volumetric analysis was performed using stereology and region-based thresholding.

Results. Excellent accuracy and intraobserver and interobserver reproducibility were demonstrated. Anatomic (total kidney volume, total cyst volume, and % cyst volume), hemodynamic (RBF and RVR), and functional (GFR) parameters were strongly correlated. Left polycystic kidneys were larger and had more severe disease. Regression analysis showed that age, diagnosis of hypertension, anatomic parameters and hemodynamic parameters were significant predictors of GFR. Multiple linear regression analysis identified age and hemodynamic parameters only as separate predictors of GFR. Anatomic, hemodynamic, and functional parameters discriminated between normotensive and hypertensive subjects despite antihypertensive treatments.

Conclusion. Renal hemodynamic parameters measured by MR correlate with anatomic and functional indices of disease severity, are the strongest predictors of renal function, and deserve further consideration as an outcome measure in clinical trials to guide therapy in ADPKD.

Autosomal-dominant polycystic kidney disease (ADPKD) is an inherited disorder characterized by renal cyst growth, early development of hypertension, and late occurrence of renal insufficiency [1]. A reduction in renal blood flow (RBF) occurs early and may precede the development of hypertension [2] or be found in its early stages [3–5]. Activation of the renin-angiotensin system (RAS) [2–7], increased sympathetic nerve activity [8], enhanced generation of endothelin [9–11], and impaired production of nitric oxide [12] may all contribute to renal vasoconstriction, remodeling of the microcirculation, and development of renal insufficiency. Administration of angiotensin I-converting enzyme (ACE) inhibitors to patients with normal renal function corrects only partially the reduction in RBF [3–5]. This indicates that the blockade of the RAS is not complete, that other vasoconstrictors are involved, or that fixed structural changes are already present at early stages of the disease.

Ritter and Barhr [13] demonstrated in 1929 that the number of small arteries and arterioles was greatly reduced in polycystic kidneys. Schacht [14, 15] in 1930 and

[1]Thomas Andreoli, M.D., served as Guest Editor for this paper.

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Key words: autosomal-dominant polycystic kidney disease, kidney volume, cyst volume, renal blood flow, renal vascular resistance, glomerular filtration rate, magnetic resonance, Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease.

1931 noted marked thickening of the media and increased wall-to-lumen ratio in small arteries and arterioles of polycystic kidneys. More recent microangiographic [16] and histopathologic studies [17] have confirmed these observations. The presence of severe nephroangiosclerosis and global glomerulosclerosis and the absence of glomerular hypertrophy and segmental glomerulosclerosis are consistent with a major role for ischemia in the progression of renal insufficiency in ADPKD.

The evaluation of RBF in ADPKD has received little attention. The few studies in this area have used measurements that rely on renal clearances of para-aminohippurate [2–5]. These assume a normal renal extraction [18], not likely in ADPKD. Recent improvements in magnetic resonance (MR) technology now allow precise direct determinations of RBF with single breath-hold MR acquisitions [19].

The National Institutes of Health (NIH)-sponsored Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) was created to develop innovative imaging techniques and analyses to follow disease progression or to evaluate treatments for ADPKD. A goal was to determine whether MR measurements of RBF can be used as a surrogate marker of disease progression. Here, we present the results obtained at the baseline visit and correlate the renal hemodynamic parameters with other clinical, anatomic, and functional indices of disease severity.

METHODS

Study organization

CRISP clinical centers included the Mayo Foundation and University of Alabama at Birmingham as a single center, Emory University, and University of Kansas Medical Center. Washington University served as the data coordinating and image analysis center (DCIAC). The DCIAC collected images transferred from the collaborating institutions in Digital Imaging and Communications in Medicine (DICOM) format, segmented and analyzed the images, stored and recorded the results using a state-of-the-art Web-based system, and performed statistical analysis. MR determinations of RBF were performed only at the Mayo Foundation and Emory University. MR studies were performed on a Signa CV/I 1.5T scanner (GE Medical Systems, Milwaukee, WI, USA) at the Mayo Foundation and on a Gyroscan Intera 1.5 T scanner (Philips Medical Systems, Best, The Netherlands) at Emory University.

Validation studies for MR flow measurement

A polyvinyl alcohol (PVA) phantom was used to validate steady flow measurements by MR imaging. PVA is material with a solid gel consistency, sufficiently firm to attach to a flow loop system. It contains free protons to yield a nonzero MR imaging signal, simulating vessel lumen in in vivo studies [20]. A block of PVA was constructed with six circular channels with diameters ranging 3.18 to 11.25 mm (range of adult human renal artery internal diameters). A 60:40 water/glycerin mixture was used to simulate blood viscosity. Measurements were obtained at flow rates that correspond with values from the literature for renal arterial blood flow (200 to 1200 mL/min), using the clinical MR protocol described below [21]. Cardiac triggering of the MR acquisition was performed using built-in physiology simulation software. True flow was determined by weighing the return from the phantom flow loop over a 1-minute interval. A second pulsatile flow phantom was designed to evaluate MR measurements of dynamic flow. It consisted of a standard cardiac pump device to create pulsatile flow through clear plastic tubings measuring 5 mm (main renal artery) or 2 mm (small accessory artery) in diameter. It used tap water as flow medium and simulated systolic and diastolic velocity variations with average flow rates of 540, 315, and 145 mL/min. Flows were measured three times in each tube at different flow rates.

Reproducibility was evaluated through blinded repeated analysis of renal arterial flow data sets from patients with single renal arteries.

Study protocol

ADPKD subjects were eligible for enrollment if they were older than 15 years of age and younger than 46 years of age and had a measured or estimated creatinine clearance >70 mL/min. ADPKD was defined by the criteria of Ravine et al [22]. Subjects were ineligible if they had undergone renal surgery, had cyst drainage procedures, were unable to undergo breath-hold MR imaging or had other medical conditions potentially affecting renal function. Hypertension was defined as a previous diagnosis and current use of antihypertensive medications or as systolic and diastolic blood pressures >140/90 mm Hg on three consecutive visits.

Enrolled subjects were scheduled for a 2-day evaluation in the General Clinical Research Center after signing an informed written consent. They were instructed to continue their medications, to discontinue any nonsteroidal anti-inflammatory medications for at least 7 days prior to evaluation, and not to initiate diuretic therapy within 14 days of evaluation. During the day prior to admission, subjects collected a 24-hour urine sample for determination of creatinine, sodium, and albumin excretions. Weight and height were measured at admission. Blood pressures were measured in the morning, prior to antihypertensive medication intake, in the left and right arms after being seated for at least 5 minutes on three occasions 3 minutes apart using an oscillometric

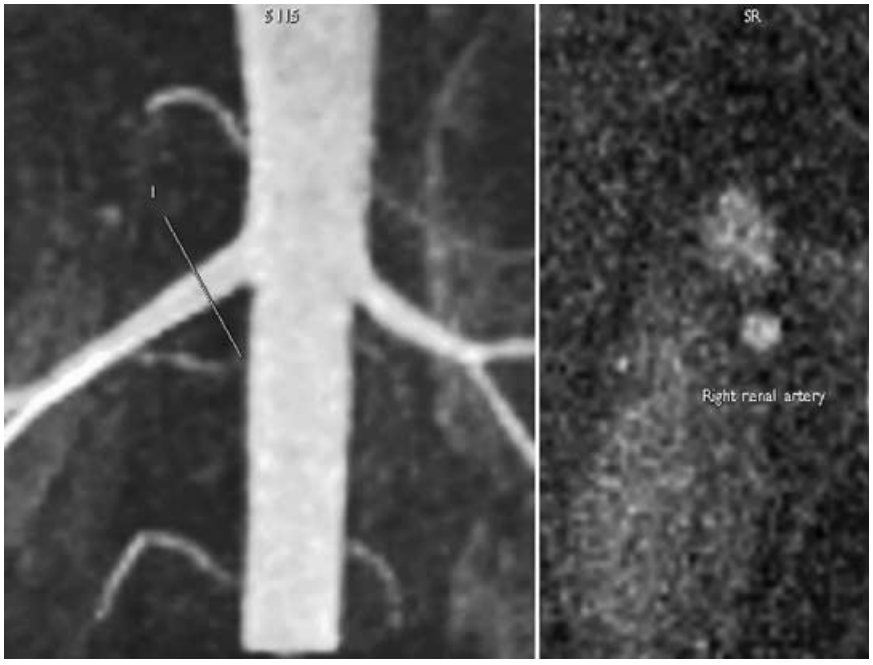

Fig. 1. Magnetic resonance (MR) angiogram of the renal arteries in a patient with autosomal-dominant polycystic kidney disease (ADPKD). (*A*) Following the MR angiogram a flow acquisition MR pulse sequence (see **Methods** section for detailed description) is performed perpendicular to the renal artery. (*B*) The flow acquisition pulse sequence yields a set of cross-sectional images through the renal arteries and veins. Flow analysis is performed on the MR signal information contained within the renal artery.

measuring device. Blood was obtained prior to glomerular filtration rate (GFR) studies for the determination of blood hemoglobin, serum electrolytes, liver enzymes, and lipid profiles using standard laboratory techniques. GFR was measured by a nonradiolabeled iothalamate clearance technique with sonographic monitoring of bladder emptying [23, 24].

MR imaging

Studies were in the morning prior to medication intake and breakfast. A 20-gauge intravenous angiocatheter was kept open with normal saline solution. Electrocardiographic pads or a peripheral gating pulsometer were positioned for ECG gating. A phased-array surface coil was positioned with its center over the inferior costal margin. An initial spoiled gradient echo scan and sequence was performed to localize the kidneys. Breath-hold coronal T2-weighted images (SSFSE/HASTE) with fat saturation were obtained with 3 and 9 mm fixed slice thickness, as well as an adjusted slice thickness attained with a single breath-hold. Neighboring image groups, necessary to cover the entire kidney, were overlapped by one slice. Coronal T1-weighted images (three-dimensional TFE/FMPSPGR), without fat saturation, with 3 mm fixed slice thickness, were obtained. Then, a three-dimensional gadolinium-enhanced (1 mL/sec for a total of 20 to 30 mL, 0.1 mmol/kg) MR angiography was performed using a standard fast-spoiled gradient echo sequence. A delay between injection and initiation of MR angiography sequence was chosen to ensure that central lines of K space were acquired during peak arterial enhancement. Coronal T1-weighted images of the kidneys were repeated at 120 to 180 seconds after beginning of the injection.

Measurements of RBF by MR imaging

Thick section oblique axial two-dimensional phase-contrast breath-hold MR angiograms were obtained along the course of each renal artery and acted as reference images (Fig. 1). The MR flow measurements were obtained perpendicular to the oblique axial two-dimensional reference images of the renal arteries utilizing a cardiac-gated, two-dimensional, fast gradient echo, phase-contrast pulse sequence. MR blood flow pulse sequence parameters were TR = 8 to 10 msec, TE = 3 to 5 msec, FOV = 14 to 20 cm, flip angle = 20 degrees, 5 mm slice thickness, 224 to 256 phase encodings, one excitation, 18-second scan time, with retrospective cardiac gating and flow compensation at 20 phases of the cardiac cycle (General Electric) or TR = 18 to 36 msec, TE = 8 to 16 msec, FOV = 20 cm, flip angle = 35 degrees, 5 mm slice thickness, 160 to 224 phase encodings, one excitation, 20- to 27-second scan time, with cardiac gating at 12 phases of the cardiac cycle (Philips). Velocity encoding value was 100 cm/sec and flow acquisition was obtained in the slice direction. Flow analysis was performed utilizing FLOW software (Medis, Inc., Leiden, The Netherlands). Semiautomated or manual techniques were employed for definition of the vessel borders in the flow images depending on image quality. Vessel area estimations were made in images at all phases of the cardiac cycle. Average maximal and minimal cross-sectional

vessel areas, peak systolic and end diastolic velocities, and flow values for each renal artery were measured. Renal vascular resistance (RVR) and resistive index (RI) were calculated using accepted formulas [25, 26].

Cyst and renal volume measurements

Kidney volumes were measured from T1-weighted images using stereology [27] and renal cyst volumes from T2-weighted images using region-based thresholding. The reliability and reproducibility of these techniques in ADPKD are described in detail elsewhere [28]. Stereology is a method of segmenting an object by counting the number of intersections of a randomly oriented and positioned grid over the object. Region-based thresholding utilizes an interactive selection of a threshold by an analyst using T2-weighted images. Cysts are brighter than the renal parenchyma in T2-weighted images and are segmented from voxels with intensity values greater than the threshold. Total kidney and cyst volumes were calculated from sets of contiguous images by summing the products of the area measurements and the slice thickness. Percent cyst volume was determined from the ratio of cyst volume to renal volume [29–32].

Statistical methods

The data were examined using SAS system software (SAS Institute, Inc., Cary, NC, USA 2002). Percent errors for phantom MR flow measurements were calculated and expressed as mean ± SD for each condition [33]. MR flow studies of 127 patients were included in computations. Comparisons between groups were performed using *t* tests. Comparisons within persons (right vs. left) were performed using dependent-samples *t* tests. Correlations were computed as Pearson *r* values. Regression analyses are simple linear regressions.

RESULTS

Phantom and reproducibility studies

Steady-flow measurements with the PVA showed that accuracy was strongly related to the phase-encoding pixel resolution. Correlation coefficients (R^2) for true/measured flow ranged from 0.77 (350 mm FOV, 96 views, pixel resolution 3.6 mm) to 0.99 (160 mm FOV, 192 views, pixel resolution 0.83 mm). Relative measurement errors for a range of vessel sizes of 0.8 to 3.8 pixels, averaged across flow rates, ranged from 112% down to 1.55%. Measurement errors below 10% were reliably obtained in phantom experiments with 200 mm FOV and 192 or more phase-encoding views per image. Pulsatile-flow measurements were performed three times and averaged by each of two radiologists. The actual and estimated flow rates and the percent error of the estimated flow rates for different tubing sizes and FOVs are summarized in Table 1.

Table 1. Accuracy of renal blood flow magnetic resonance (MR) measurements by two radiologists using a flow phantom

Tubing size *mm*	Field of view *cm*	Actual flow rate *mL/min*	Estimated flow rate *mL/min*	Error %
5	14	315	313,322	0.6–2.2
5	14	540	545,530	0.9–1.9
5	20	315	313,311	0.6–1.2
5	20	540	554,562	2.8–4.1
2	14	145	134,125	7.6–13.8
2	20	145	143,149	1.4–2.8

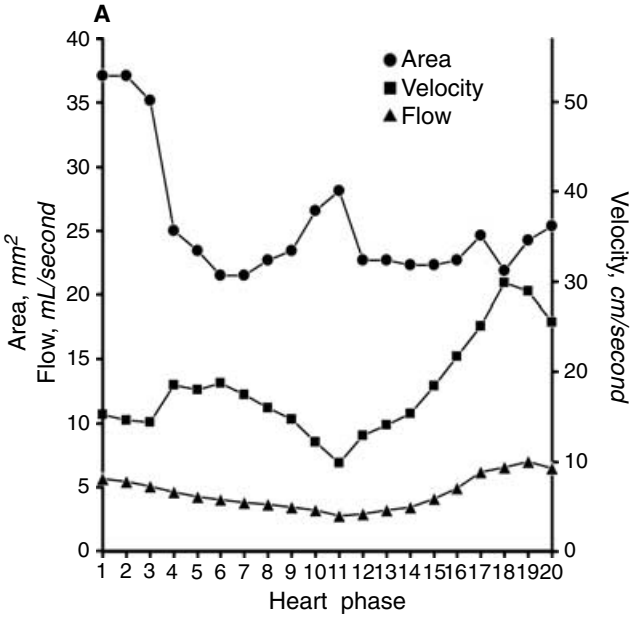

Fig. 2. Analyses of patient with autosomal-dominant polycystic kidney disease (ADPKD). (*A*) Velocity, cross-sectional area, and blood flow plotted during 20 phases of the cardiac cycle in the left renal artery in a magnetic resonance (MR) flow acquisition of an ADPKD patient. (*B*) Cross-sectional flow acquisition images in the left renal artery of the same patient.

These showed 0.6% to 4.1% errors of estimated flow rates, using 14 or 20 cm FOVs, for a 5 mm tubing and actual flow rates of 315 or 540 mL/min, and 1.4% to 13.8% errors for a 2 mm tubing and actual flow rates of 145 mL/min.

Based on the results of the phantom studies, MR renal blood flow acquisitions were optimized in patients utilizing a FOV of 20 cm or less and at least 192 phase-encoding steps. A representative sample of data recorded during the cardiac cycle is illustrated in Figure 2. The average intrareviewer coefficient of variation (CV) of total RBF measurements performed three times by two radiologists in 19 patients (Fig. 3) was 1.4% for reviewer A and 1.2% for reviewer B. The estimated reliability (intraclass correlation coefficient) for reviewer A was 0.987 and 0.983 for reviewer B. Using within patient replication means, the average interreviewer CV was 2.5% with a reliability coefficient of 0.983.

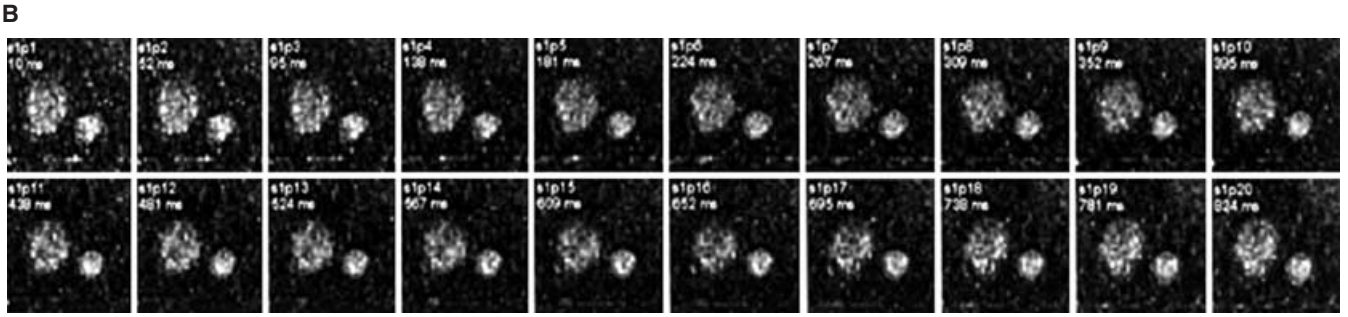

Fig. 2. (Continued).

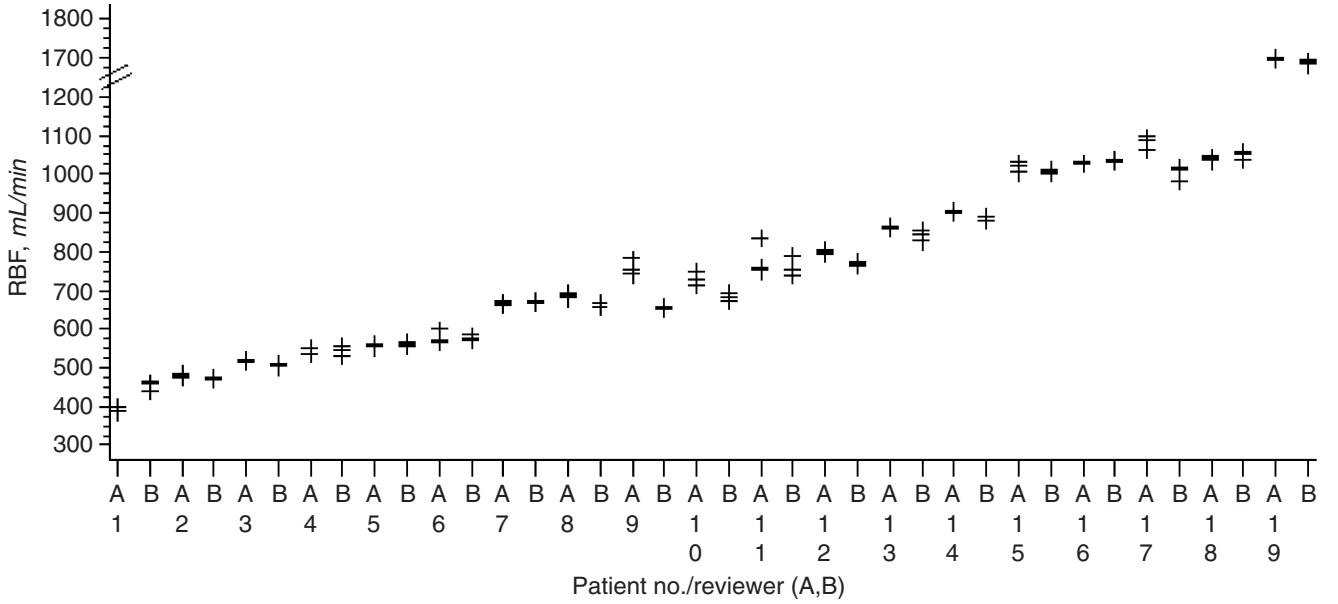

Fig. 3. Blood flow measurements repeated three times in 19 autosomal-dominant polycystic kidney disease (ADPKD) patients by radiologists A and B. The intrareviewer coefficients of variation were 1.2% and 1.4%. The average interreviewer coefficient of variation was 2.5%.

Description of anatomic, hemodynamic, and functional data

The 127 subjects in the study, 46 male and 81 female, had an age of 32.9 ± 8.2 years, a mean arterial pressure of 96.3 ± 10.8 mm Hg, and an iothalamate clearance of 99.1 ± 23.0 mL/min/1.73 m^2. Forty of them (31.5%) had multiple renal arteries, bilaterally in six and unilaterally in the rest. Women had lower systolic blood pressures, hematocrits, serum concentrations of creatinine and triglycerides, and urine sodium excretions, and higher serum concentration of high-density lipoprotein (HDL) cholesterol than men. Right and left renal volumes and hemodynamic parameters are compared in Table 2. Left kidneys were larger than right kidneys and had more severe disease. RBF and peak systolic and end diastolic velocities were lower and RVR was higher in the left kidneys, while RI was similar in both kidneys.

Table 2. Comparison of right and left renal volumes and hemodynamic parameters ($N = 127$)

	Right	Left	*P* value
Kidney volume *mL*	498.4 ± 309.5	554.5 ± 344.3	<0.001
Cyst volume *mL*	234.4 ± 230.9	275.4 ± 272.6	0.001
% Cyst volume	38.3 ± 18.4	40.5 ± 18.6	0.047
Renal blood flow *mL/min/1.73 m^2*	398.5 ± 124.4	354.7 ± 125.9	<0.001
Peak systolic velocity *cm/sec*	38.4 ± 11.7	31.7 ± 9.3	<0.001
End diastolic velocity *cm/sec*	14.3 ± 6.0	11.9 ± 7.1	<0.001
Renal vascular resistance *dynes sec.cm^{-5}*	21332 ± 7750	25164 ± 11662	<0.001
Resistive index	0.63 ± 0.11	0.62 ± 0.18	NS

Correlations between total or ipsilateral kidney volumes and renal hemodynamic parameters

These correlations are summarized in Table 3. Total kidney volume, total cyst volume, and % cyst volume

Table 3. Correlations of total or ipsilateral kidney volumes with functional or hemodynamic parameters

	Kidney volume		Cyst volume		% Cyst volume	
	r	*p*	*r*	*p*	*r*	*P*
Age	0.388	<0.001	0.392	<0.001	0.434	<0.001
Mean arterial pressure	0.284	0.001	0.276	0.003	0.259	0.023
Both kidneys						
Iothalamate clearance	−0.314	<0.001	−0.330	<0.001	−0.368	<0.001
Blood flow	−0.344	<0.001	−0.377	<0.001	−0.434	<0.001
Vascular resistance	0.450	<0.001	0.467	<0.001	0.482	<0.001
Right kidney						
Blood flow	−0.241	0.006	−0.267	0.002	−0.353	<0.001
Peak systolic velocity	−0.167	0.057	−0.199	0.028	−0.197	0.043
End diastolic velocity	−0.247	0.005	−0.297	<0.001	−0.318	0.001
Vascular resistance	0.339	<0.001	0.351	<0.001	0.419	<0.001
Resistive index	0.219	0.013	0.262	0.003	0.274	0.002
Left kidney						
Blood flow	−0.382	<0.001	−0.428	<0.001	−0.439	<0.001
Peak systolic velocity	−0.182	0.042	−0.190	0.050	0.129	NS
End diastolic velocity	−0.261	0.003	−0.279	0.002	−0.336	<0.001
Vascular resistance	0.541	<0.001	0.584	<0.001	0.500	<0.001
Resistive index	0.227	0.011	0.246	0.008	0.327	<0.001

correlated positively with age, blood pressure, and RVR, and negatively with GFR and RBF. Right and left kidney volumes, cyst volumes, and percent cyst volumes were inversely correlated with the ipsilateral RBF and end diastolic velocity and positively correlated with RVR and RI.

RBF as a predictor of GFR

Iothalamate clearances were significantly higher in normotensive than hypertensive subjects (see below). In addition, they were inversely correlated with age ($r = -0.390$, $P < 0.001$) and kidney volume (see above) and positively correlated with RBF ($r = 0.5172$, $P < 0.001$). The regression analysis shown in Table 4 uses age, gender, diagnosis of hypertension, kidney volume, and RBF to predict GFR. When considered alone (as measured by the Pearson correlation *r*), age, diagnosis of hypertension, kidney volume, and RBF were all significant predictors. In the multiple-variable model, however, only age and RBF were significant independent predictors. The R^2 value of 0.3417 was relatively large. If *r* for RBF in the univariate analysis (0.5172) is squared, the ratio $0.5172^2/0.3417 = 0.783$. Therefore, RBF alone accounted for almost 80% of the variance in the model. Both GFR and RBF were corrected for body surface area (BSA). To ensure that this correction was not inducing a relationship, uncorrected versions of these variables were used. The results were almost exactly the same, with $R^2 =$ 0.346 and the same significant variables. Similar results were obtained if RBF was replaced by RVR or if total kidney volume was replaced by total cyst volume or percent cyst volume.

Table 4. Regression model predicting glomerular filtration rate (GFR): Effect of age, gender, physical kidney measures, and renal blood flow

Source	F Value	*P* value	*r* value	*P* value
Age	6.16	0.0145	−0.3948	0.0001
Gender	2.37	0.1260	0.0733	0.3894
Diagnosis of hypertension	0.11	0.7394	−0.1883	0.0347
Total kidney volume	0.50	0.4827	−0.2918	0.0014
Total corrected renal blood flow	27.80	<0.0001	0.5172	0.0001

Total kidney and cyst volumes and renal hemodynamic parameters in hypertensive and normotensive subjects and effects of treatment

These parameters are presented in Table 5. Hypertensive had significantly higher RVR than normotensive subjects. Of the 74 patients with hypertension, 52 were treated with ACE inhibitors or angiotensin receptor blockers, eight with beta blockers, seven with calcium channel blockers, and eight with diuretics. The subjects treated with ACE inhibitors/angiotensin receptor blockers had significantly lower mean arterial pressures and those treated with calcium channel blockers significantly higher pulse pressures than those not taking these medications. There was a statistically nonsignificant trend toward higher RBF and GFR in the subjects treated with ACE inhibitors/angiotensin receptor blockers or with calcium channel blockers, whereas the reverse was true for those taking beta blockers or diuretics.

DISCUSSION

The results of the present study demonstrate that breath-hold gradient-echo techniques used with current imaging equipment provide adequate resolution for accurate measurements of RBF in phantoms simulating renal artery hemodynamics and for reproducible measurements of RBF in patients with ADPKD. Using this technology, we studied 127 CRISP participants and demonstrated that renal hemodynamic parameters measured by MR are significantly correlated with anatomic and functional indices of disease severity. Age, diagnosis of hypertension, total kidney, total cyst, and percent cyst volumes, RBF and RVR were significantly correlated with GFR. The regression analysis, however, indicated that age and renal hemodynamic parameters (RBF and RVR), but not kidney volumes, were independent predictors of GFR. These results strongly suggest that RBF and RVR measured by MR deserve further consideration

Table 5. Total kidney volumes and renal hemodynamic parameters in normotensive compared to hypertensive subjects and effects of antihypertensive medications

Blood pressure	Number	Age *years*	Total kidney volume *mL*	Mean arterial pressure *mm Hg*	Systolic blood pressure-diastolic blood pressure *mm Hg*	Renal blood flow *mL/min/1.73 m²*	Renal vascular resistance *dynes sec.cm⁻⁵*	Glomerular filtration rate *mL/min/1.73 m²*
Normotensive	53	29.2 ± 7.7	731 ± 406	91.7 ± 9.4	38.8 ± 7.2	783 ± 205	9965 ± 2646	104.2 ± 19.2
Hypertensive	74	34.5 ± 7.6	1284 ± 673	99.6 ± 10.6	38.6 ± 8.3	732 ± 243	12135 ± 4383	95.5 ± 24.9
P value		<0.001	<0.001	<0.001	NS	NS	0.002	0.035
On ACE inhibitors/ARB[a]	52	35.5 ± 8.2	1343 ± 726	97.0 ± 10.4	38.3 ± 6.3	746 ± 258	11701 ± 4502	97.8 ± 24.8
Without ACE inhibitors/ARB[a]	22	35.0 ± 6.2	1143 ± 516	105.8 ± 8.5	39.5 ± 12.1	699 ± 206	13160 ± 3997	89.9 ± 24.9
P value		NS	NS	<0.001	NS	NS	NS	NS
On calcium channel blockers[a]	7	29.2 ± 8.6	779 ± 236	100.5 ± 9.2	47.1 ± 8.9	823 ± 226	10415 ± 2889	112.0 ± 31.0
Without calcium channel blockers[a]	67	36.0 ± 7.3	1336 ± 683	99.6 ± 10.8	37.8 ± 7.8	722 ± 245	12314 ± 4488	93.7 ± 23.8
P value		0.022	0.040	NS	0.004	NS	NS	NS
On beta blockers[a]	8	36.8 ± 8.0	1177 ± 370	102.8 ± 6.2	38.2 ± 8.1	594 ± 132	14404 ± 3175	84.4 ± 18.1
Without beta blockers[a]	66	35.3 ± 7.6	1296 ± 702	99.3 ± 11.0	38.7 ± 8.4	748 ± 249	11860 ± 4447	96.6 ± 25.3
P value		NS	NS	NS	NS	0.091	0.122	NS
On diuretic*	8	40.3 ± 7.5	1439 ± 706	99.7 ± 8.9	35.2 ± 9.5	607 ± 83	13430 ± 2620	86.3 ± 10.5
Without diuretic*	66	34.9 ± 7.6	1264 ± 673	99.6 ± 10.8	39.1 ± 8.2	744 ± 252	11978 ± 4539	96.6 ± 26.0
P value		NS	NS	NS	NS	NS	NS	NS

Abbreviations are: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers
[a]Hypertensive only.

as an outcome measure in treatment trials for ADPKD. These cross-sectional observations, however, need to be validated by a prospective longitudinal follow-up study.

The results also indicate that renal hemodynamic and functional parameters discriminate between normotensive and hypertensive ADPKD subjects, despite administration of antihypertensive therapies. Statistically nonsignificant trends toward higher RBF and lower RVR were observed in subjects treated with ACE inhibitors, angiotensin receptor blockers, or calcium channel blockers, whereas the reverse was true in those receiving beta blockers or diuretics. Their interpretation should be extremely cautious, because of small sample sizes, simultaneous utilization of several antihypertensive agents in a few patients, and variable durations of therapy. Nevertheless, they raise the possibility that measurements of renal hemodynamic parameters by MR might help in the selection or optimization of antihypertensive therapy in ADPKD.

The higher volume of the left polycystic kidneys is not entirely unexpected. The left kidney is slightly larger than the right, 136 mL compared to 123 mL or 10% larger, as measured by computed tomography in healthy subjects [34] and previously reported in autopsy studies [35]. In the present study, the left polycystic kidney is also approximately 10% larger than the right. However, the severity of the polycystic kidney disease in the left kidneys, as reflected by higher cystic involvement, reduced RBF and higher RVR, seems out of proportion to the relative increase in total kidney volume. This may suggest that factors determining the difference in right and left kidney volumes in normal individuals may also influence the progression of the cystic disease. The left renal artery originates from the aorta at a slightly higher level than the right renal artery. In normal subjects, blood flow to the left kidney is slightly higher than flow to the right kidney, but renal perfusion, taking into account renal volumes, is identical for both kidneys [34]. Nevertheless, it is possible that subtle developmental or hemodynamic differences between the kidneys could have an effect on the progression of the disease.

RI measured by Doppler ultrasonography has been frequently used to estimate RVR in renal allografts and in native kidneys [36–39]. In one study of patients with ADPKD, RI was found to correlate with morphologic and functional indices of disease severity [40]. The present study confirms that RI measured by MR correlates with total kidney volume, cyst volume, and percent cyst volume. However, the correlation was weaker than that between RVR and renal volumes. In addition, RI was similar in the right and left polycystic kidneys despite significant differences in RVR. This is likely due to the dependency of RI on other variables such as arterial compliance and pulse pressure [41, 42].

CONCLUSION

This study shows that novel MR technologies allow a real-time, noninvasive assessment of renal hemodynamic parameters. The capability to accurately assess the renal circulation by MR has great potential for investigation of the role of hemodynamic alterations in renal disease progression, not only in ADPKD, but also in other renal diseases.

ACKNOWLEDGMENTS

The authors greatly appreciate the assistance of the study coordinators, LaFave Dean, B.Sc., Lorna Stevens, R.N., and Diane Watkins, M.A.S., and thank Jesse Davila, M.D., David Frakes, B.Sc., Ashley Wallin, B.Sc., and Professor Ajit Yoganathan for their help and advice. This work was supported by National Institutes of Health grant DK56957, Mayo Clinic General Clinical Research Center grant MO1-RR00585, and Emory University General Clinical Research Center grant MO1-RR00039.

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