MR-derived renal morphology and renal function in patients with atherosclerotic renovascular disease

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Appropriate selection of patients with atherosclerotic renovascular disease (ARVD) for revascularization might be improved if accurate non-invasive investigations were used to assess severity of pre-existing parenchymal damage. The purpose of this study was to evaluate the associations between magnetic resonance imaging (MRI)-measured renal morphological parameters and single-kidney glomerular filtration rate (GFR) in ARVD. Three-dimensional (3D)-MRI was performed on 35 ARVD patients. Renal bipolar length (BL), parenchymal volume, parenchymal (PT), and cortical thicknesses (CT) were measured in 65 kidneys. Thirteen kidneys were supplied by normal vessels, 13 had insignificant ($<50\%$) renal artery stenosis (RAS), 33 significant ($\geqslant 50\%$) RAS, and six complete vessel occlusion. All patients underwent radioisotopic measurement of single-kidney GFR (isoSK-GFR). Overall, 3D parameters such as parenchymal volume were better correlates of isoSK-GFR ($r=0.86$, $P<0.001$) than BL ($r=0.78$, $P<0.001$), PT ($r=0.63$, $P<0.001$) or CT ($r=0.60$, $P<0.001$). Kidneys with $\geqslant 50\%$ RAS did show significant reduction in mean CT compared to those supplied by normal vessel (5.67 ± 1.63 vs 7.28 ± 1.80 mm, $P=0.002$; 22.1% reduction) and an even greater loss of parenchymal volume (120.65 ± 47.15 vs 179.24 ± 86.90 ml, $P<0.001$; 32.7% reduction) with no significant reduction in BL. In a proportion of $\geqslant 50\%$ RAS kidneys, a disproportionately high parenchymal volume to isoSK-GFR was observed supporting a concept of 'hibernating parenchyma'. 3D parameters of parenchymal volume are stronger correlates of isoSK-GFR than two-dimensional measures of BL, PT or CT. 3D morphological evaluation together with isoSK-GFR might be useful in aiding patient selection for renal revascularization. Kidneys with increased parenchymal volume to SK-GFR might represent a subgroup with the potential to respond beneficially to angioplasty.

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Atherosclerotic renovascular disease (ARVD) is commonly associated with hypertension,[1] chronic, and end-stage renal disease,[2,3] and various cardiovascular pathologies such as coronary artery disease and cardiac failure.[4,5] Renal revascularization procedures are widely used in an attempt to modify the natural history of some of these conditions,[6] but renal functional outcomes are variable and often unpredictable in individual patients,[7–9] reflecting the heterogeneous renal injury responsible for the renal dysfunction in ARVD.[10–14] Appropriate patient selection for revascularization would be improved if accurate non-invasive investigations were used to assess the degree of pre-existing renal parenchymal damage, as these might help predict the clinical response to angioplasty in the kidney with renal artery stenosis (RAS). However, there is currently no consensus regarding the most useful investigations, and where predictive benefits have been demonstrated with certain techniques (e.g. measurement of resistive index with Doppler ultrasound[15]), these have not been widely utilized.

Analysis of renal morphology, most often by simple ultrasound measurement of renal bipolar length, is the most common means of estimating the extent of parenchymal damage in RAS.[16,17] More detailed renal morphological parameters, such as renal volume and the thickness of the total parenchyma or renal cortex, have been used to predict overall renal function in normal individuals and in those with chronic renal disease.[18–20] Cortical thickness and cortical area have been shown to predict the presence of unilateral RAS with far greater sensitivity and accuracy than renal bipolar length in patients with early ARVD or fibromuscular dysplasia.[21,22] Despite RAS frequently being unilateral, no studies have attempted to relate measures of morphology to individual kidney function, rather utilizing estimated glomerular filtration rate (GFR) as the functional parameter, which calculates global rather than individual kidney function.

Gadolinium-enhanced magnetic resonance (MR) angiography (MRA) is becoming the method of choice for investigation of RAS as it is non-invasive and it avoids the risks of contrast nephropathy that may complicate other contrast radiographic techniques,[23] and detailed assessment of renal morphology can be acquired during the same MRA study.[24] We therefore examined the association of renal

bipolar length, parenchymal volume, and cortical thickness measured with gadolinium-enhanced magnetic resonance imaging (MRI) with radioisotopic single-kidney GFR (isoSK-GFR) in patients with ARVD.

RESULTS

During the recruitment period, 35 patients with ARVD were investigated. Two patients were previously known to have single kidneys. There was one patient who had bilateral multiple cortical infarcts, which precluded accurate measurement of cortical thickness and therefore was excluded from analysis. Another patient had a severely atrophic kidney with multiple large degenerative cysts and this kidney was not included in the data analysis. Hence, a total of 65 kidneys were studied. The mean patient age was 70.3 ± 7.4 years (range 50–81.1 years), and 24 were male and 10 female. MRA showed that 13 kidneys were supplied by normal vessels, 13 by vessels with insignificant RAS, 33 by significant RAS, and six had complete occlusion (RAO).

Correlation between renal morphology and isoSK-GFR

Fifty-nine kidneys were included in the correlation analysis (RAO kidneys excluded). The relationships between bipolar length (Figure 1), parenchymal volume (Figure 2), mean parenchymal thickness (MPT) (Figure 3), mean cortical thickness (MCT) (Figure 4), and isoSK-GFR are shown. Overall, all morphological parameters were significantly correlated with isoSK-GFR. Statistically, isoSK-GFR was better correlated with renal parenchymal volume ($r = 0.86$, $P < 0.001$) than with bipolar length ($r = 0.78$, $P < 0.001$) or MPT and MCT ($r = 0.63$, $P < 0.001$; $r = 0.60$, $P < 0.001$, respectively). IsoSK-GFR was more strongly correlated with estimated cortical mass ($r = 0.79$, $P < 0.001$) than with MCT (Figure 5). In the subanalysis of normal vessel/insignificant RAS kidneys, all morphological parameters were significantly correlated with isoSK-GFR, with a stronger correlation with parenchymal volume ($r = 0.86$, $P < 0.001$) than bipolar length ($r = 0.81$, $P < 0.001$), MPT ($r = 0.68$, $P < 0.001$) or MCT ($r = 0.73$, $P < 0.001$). Of the significant RAS kidneys, again the strongest correlation with isoSK-GFR was seen with parenchymal volume ($r = 0.76$, $P < 0.001$) compared to bipolar length ($r = 0.65$, $P < 0.001$), but there was no

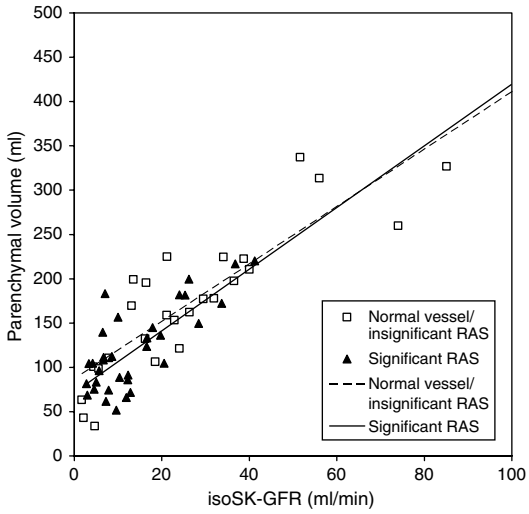

Figure 2 | Correlation regression for renal parenchymal volume and isoSK-GFR. Overall, renal volume was significantly related to GFR ($r = 0.86$, $P < 0.001$). Correlation subanalysis showed significant correlations in the normal vessel/insignificant RAS ($n = 26$; $r = 0.86$, $P < 0.001$) and significant RAS ($n = 33$; $r = 0.76$, $P < 0.001$) groups.

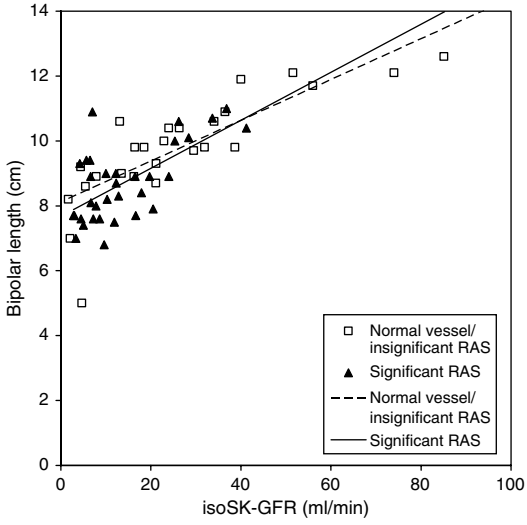

Figure 1 | Correlation regression for bipolar length and isoSK-GFR. Overall ($n = 59$), bipolar length was significantly correlated with GFR ($r = 0.78$, $P < 0.001$). Correlation subanalysis showed significant correlations in the normal vessel/insignificant RAS ($n = 26$; $r = 0.81$, $P < 0.001$) and significant RAS ($n = 33$; $r = 0.65$, $P < 0.001$) groups.

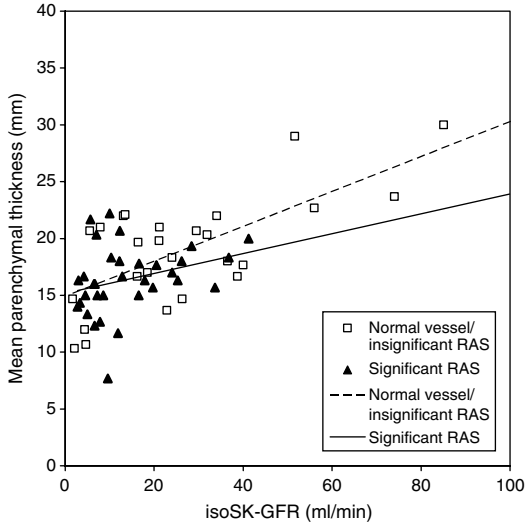

Figure 3 | Correlation regression for parenchymal thickness and isoSK-GFR. Overall, parenchymal thickness was significantly related to GFR ($r = 0.63$, $P < 0.001$). Correlation subanalysis showed significant correlation in the normal vessel/insignificant RAS group ($n = 26$; $r = 0.68$, $P < 0.001$), but not in significant RAS group ($n = 33$; $r = 0.30$, NS).

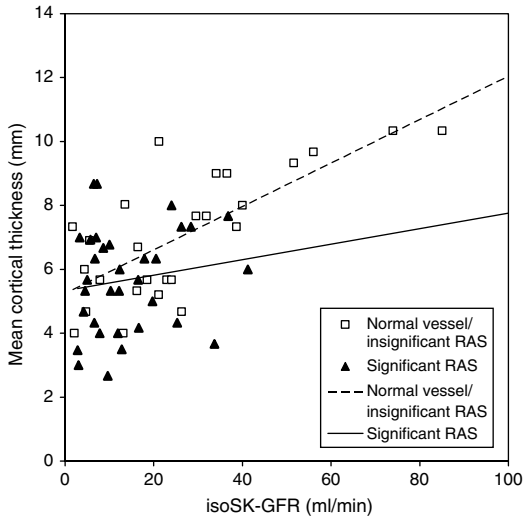

Figure 4 | Correlation regression for cortical thickness and isoSK-GFR. Overall, cortical thickness was significantly related to GFR ($r = 0.60$, $P < 0.001$). Correlation subanalysis showed significant correlation in the normal vessel/insignificant RAS group ($n = 26$; $r = 0.73$, $P < 0.001$), but not in significant RAS group ($n = 33$; $r = 0.15$, NS).

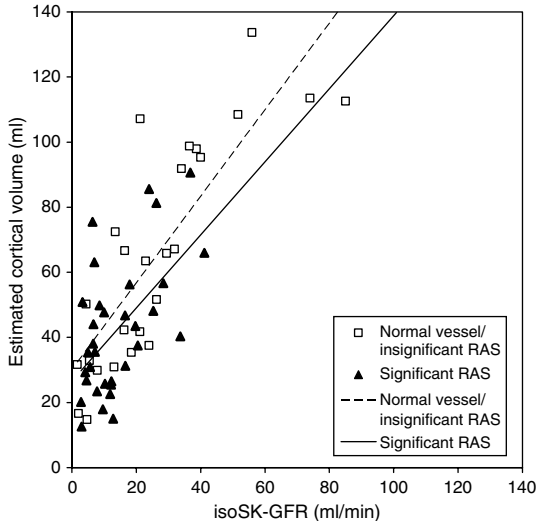

Figure 5 | Correlation regression for estimated cortical mass and isoSK-GFR. Overall, cortical mass was significantly related to GFR ($r = 0.79$, $P < 0.001$). Correlation subanalysis showed significant correlations in the normal vessel/insignificant RAS ($n = 26$; $r = 0.83$, $P < 0.001$) and significant RAS ($n = 33$; $r = 0.57$, $P < 0.001$) groups.

correlation with other two-dimensional (2D) structural parameters.

Renal morphology differences and severity of renovascular disease

Overall, kidneys supplied by significant RAS were significantly smaller in volume and had thinner cortices than those supplied by normal vessels ($P < 0.001$) (Table 1). Although the mean bipolar length of kidneys with significant RAS was approximately 10% smaller than mean lengths of kidneys in the other two groups, this difference was not statistically significant. When patient height, body mass index or surface area was compared between the groups, no differences could be identified.

Morphological and functional characteristics of small kidneys

Table 2 compares the morphological and functional characteristics of kidneys with significant RAS grouped according to whether they were small (bipolar length < 8 cm, or of preserved size). As expected, there were significant corresponding reductions in volume, estimated cortical mass, parenchymal, and medullary thicknesses in the kidneys with smaller length, but six (54.5%) small kidneys had isoSK-GFR $\geqslant 7$ ml/min. The subanalysis of morphological parameters of these 11 kidneys grouped according to function (isoSK-GFR $\geqslant 7$ ml/min group ($n = 6$) vs < 7 ml/min group ($n = 5$)) showed no difference in all morphological characteristics (Table 3) despite a significant difference in mean isoSK-GFR between groups. The parenchymal volume to isoSK-GFR ratio was used to estimate the degree of preservation of renal tissue in relation to function. Although there was no overall difference in this parameter between significant RAS and normal vessel/insignificant RAS kidneys (Table 1), subanalysis of the 11 small kidneys in the significant RAS group (Table 3) showed that kidneys with low GFR had a significantly greater parenchymal volume: isoSK-GFR (23.4 ± 6.8 vs 7.6 ± 3.0 ml per ml/min of GFR, $P = 0.001$).

DISCUSSION

Renal morphology should always be considered in the clinical evaluation of patients with renovascular disease. The length of a kidney is often used as an aid to the diagnosis of ARVD, but also as a surrogate to estimate function and assess viability. As renal functional outcomes are known to vary after revascularization, it is important to focus attention on improving the identification of those ARVD patients in whom a beneficial change in renal function will accompany revascularization. This study adds further to our understanding of which renal structural parameters are most strongly linked to individual kidney function with three-dimensional (3D) morphological parameters being more closely related to individual kidney function than 2D parameters.

Few previous investigators have studied renal morphology in relation to individual kidney function in any form of renal disease. Most studies have used estimated GFR calculated from serum creatinine values, and this represents overall bilateral rather than individual kidney function. We have estimated the GFR of each kidney by a standard radioisotopic method that is both accurate and reliable.[26] In this study, we noted that bipolar length, parenchymal volume, parenchymal, and cortical thicknesses all showed some correlation with isoSK-GFR. Although parenchymal and cortical thicknesses are often used as markers in the assessment of intra-renal damage, we found that cortical thickness was the weakest

Table 1 | Morphological parameters and severity of renal artery stenosis

	Normal	RAS < 50%	RAS ⩾ 50%	RAO	*P*-value
Number, *n* (%)	13 (20)	13 (20)	33 (50.8)	6 (9.2)	
Renal function					
isoSK-GFR (ml/min) mean ± s.d. (range)	29.29 ± 21.51 (4.68–85.10)	24.32 ± 21.72 (1.70–74.00)	14.08 ± 10.34[a] (2.80–41.20)	1.61 ± 0.97[b, c] (0.43–2.90)	0.001
Body size					
Height (cm) mean ± s.d. (range)	167.21 ± 10.44 (150.50–182.20)	168.02 ± 8.89 (153.70–182.20)	162.84 ± 7.76 (146.80–177.50)	158.25 ± 9.81 (146.80–168.40)	0.066
BMI (kg/m^2) mean ± s.d. (range)	26.88 ± 4.56 (20.67–33.61)	26.44 ± 4.23 (20.67–33.61)	25.37 ± 3.96 (18.40–32.24)	26.10 ± 3.64 (20.95–31.73)	0.680
Body surface area (m^2) mean ± s.d. (range)	1.84 ± 0.27 (1.48–2.41)	1.87 ± 0.24 (1.52–2.41)	1.75 ± 0.21 (1.38–2.11)	1.69 ± 0.24 (1.45–2.08)	0.226
Renal morphology					
Bipolar length (cm) mean ± s.d. (range)	9.80 ± 1.86 (5.0–12.6)	9.82 ± 1.50 (7.0–12.1)	8.72 ± 1.18 (6.8–11)	6.33 ± 1.40[d] (4.0–8.0)	< 0.001
Parenchymal volume (ml) mean ± s.d. (range)	179.24 ± 86.90 (33.78–337.09)	168.52 ± 76.40 (42.99–313.43)	120.65 ± 47.15[a] (51.65–220.04)	52.01 ± 38.07[b, c] (17.3–126.55)	< 0.001
MPT (mm) mean ± s.d. (range)	19.65 ± 5.43 (10.67–30.0)	18.42 ± 4.22 (10.33–23.67)	16.39 ± 3.02 (7.67–22.2)	9.56 ± 3.94[d] (6.67–17.0)	< 0.001
MCT (mm) mean ± s.d. (range)	7.28 ± 1.80 (4.67–10.33)	6.86 ± 2.2 (4.0–10.33)	5.67 ± 1.63[a] (2.67–8.67)	3.83 ± 1.44[b] (2.0–6.0)	0.002
MMT (mm) mean ± s.d. (range)	12.37 ± 4.03 (6.0–19.67)	11.56 ± 3.60 (6.0–18.0)	10.72 ± 2.66 (5.0–15.43)	5.72 ± 3.13[d] (3.33–12.0)	0.001
Estimated cortical mass (ml)[e] mean ± s.d. (range)	67.24 ± 32.65 (14.78–112.56)	64.31 ± 37.14 (16.64–133.67)	42.44 ± 20.54[a] (12.59–90.67)	24.02 ± 23.79[b, c] (5.20–71.18)	0.002
Renal volume index[f] mean ± s.d. (range)	6.78 ± 3.69 (1.38–16.31)	6.28 ± 2.72 (2.08–10.97)	4.69 ± 1.46[a] (1.94–8.19)	1.91 ± 1.12[b, c] (0.73–3.99)	< 0.001
Parenchymal volume/isoSK-GFR ratio (ml per ml/min of GFR) mean ± s.d. (range)	10.13 ± 7.58 (3.51–37.26)		12.28 ± 7.77 (5.11–31.39)		0.290

[a]Between normal and significant RAS groups.
[b]Between normal and RAO groups.
[c]Between insignificant and RAO groups.
[d]Between RAO and all other groups.
[e]Estimated cortical mass: (cortical thickness/parenchymal thickness) × parenchymal volume.
[f]Renal volume index:[25] parenchymal volume adjusted for BMI (parenchymal volume/BMI).
Post-hoc analysis using conferroni correction: $P < 0.05$.

correlate of renal function, with kidneys supplied by significant RAS showing no correlation between isoSK-GFR and MPT or MCT. The strongest correlate of isoSK-GFR was parenchymal volume, which is not unexpected as it represents a 3D evaluation of the kidney rather than the 2D assessment provided by measurements of bipolar length or parenchymal and cortical thicknesses. The adjustment of cortical thickness measurements for the volume of the kidney (estimated cortical mass), however, improved the strength of the correlation with renal function. Furthermore, parenchymal volume was also found to be a more accurate diagnostic marker of significant ARVD than either bipolar length or cortical thickness. It is well known that renal morphology is affected by body habitus and there are correlations of renal length with height, and renal volume with height, weight, and body surface area in normal subjects.[27] In our study, no differences were found in height, body mass index or surface area between groups with differing renal artery anatomy. Nevertheless, the significant differences between the groups still existed after correction of the volume of the kidneys for body mass index (renal volume index[25]).

An asymmetry in renal length, due to atrophy of kidneys supplied by RAS, is commonly seen in patients with ARVD.[28,29] However, as shown in our study, changes in renal length may not be as sensitive as other renal morphological parameters in determining the presence of intra-renal injury in early ARVD. Using spiral computed tomography (CT) imaging, Mounier-Vehier *et al.*[21] showed that a significant decrease in cortical thickness with no measurable difference in bipolar length was noted in kidneys with RAS compared to those supplied by normal vessels, suggesting that cortical parameters are more sensitive markers for early ARVD diagnosis. The results from our study support these findings, with significant reductions in cortical thickness and parenchymal volume being associated with significant RAS, with no significant difference in bipolar length being observed. Statistically, our study showed parenchymal volume to be a more sensitive marker of the intra-renal changes due to significant RAS than MCT. However, in this study, the MCT calculation was based on three (upper, lateral, and lower measurements of cortical thickness)[24] rather than the six separate measurements used by Mounier-Vehier *et al.*[21]

Full evaluation of renal morphology required the assessment of mean medullary thickness (MMT). Interestingly, no difference was observed in MMT between kidneys supplied by significant RAS, insignificant RAS or normal vessels in this study. This may be explained by physiological adaptive mechanisms.[30]

Currently, there are no definite morphological or functional parameters that can predict a successful renal functional outcome after revascularization in ARVD, but

Table 2 | Comparison of morphology in kidneys with significant RAS grouped according to size

	<8 cm kidneys	⩾8 cm kidneys	*P*-value
Number, *n* (%)	11 (33.3)	22 (66.7)	
Renal function			
isoSK-GFR (ml/min) mean±s.d. (range)	8.46±5.85 (2.80–20.50)	16.90±11.03 (4.20–40.20)	0.024
Body size			
Height (cm) mean±s.d. (range)	152.80±6.09 (152.80–169.30)	164.27±8.23 (146.80–177.50)	0.136
BMI (kg/m^2) mean±s.d. (range)	24.52±2.88 (19.61–28.77)	26.21±3.83 (19.61–32.24)	0.084
Body surface area (m^2) mean±s.d. (range)	1.65±0.20 (1.38–1.93)	1.79±0.20 (1.45–2.11)	0.054
Renal morphology			
Bipolar length (cm) mean±s.d. (range)	7.50±0.33 (6.80–7.90)	9.32±0.95 (8.0–11.0)	<0.001
Parenchymal volume (ml) mean±s.d. (range)	85.64±24.98 (51.65–133.41)	138.08±46.16 (71.50–220.04)	0.001
MPT (mm) mean±s.d. (range)	14.35±2.85 (7.67–17.80)	17.42±2.59 (12.33–22.20)	0.004
MCT (mm) mean±s.d. (range)	5.18±1.89 (2.67–8.67)	5.91±1.46 (3.50–8.67)	0.224
MMT (mm) mean±s.d. (range)	9.17±2.79 (5.0–13.63)	11.50±2.28 (7.33–15.43)	0.015
Estimated cortical mass (ml)[a] mean±s.d. (range)	30.96±12.44 (12.59–50.89)	48.18±21.59 (15.01–90.67)	0.021

[a]Estimated cortical mass: (cortical thickness/parenchymal thickness) × parenchymal volume.

Table 3 | Morphological parameters of small kidneys with significant RAS grouped: isoSK-GFR <7 ml/min or ⩾7 ml/min

	isoSK-GFR <7 ml/min	isoSK-GFR ⩾7 ml/min	*P*-value
Number, *n* (%)	5 (45.5)	6 (54.5)	
Renal function			
isoSK-GFR (ml/min) mean±s.d. (range)	3.72±0.97 (2.80–5.0)	12.40±2.10 (7.20–20.50)	0.005
Body size			
Height (cm) mean±s.d. (range)	161.76±8.28 (152.80–169.30)	158.48±3.68 (154.10–162.80)	0.402
BMI (kg/m^2) mean±s.d. (range)	24.33±2.54 (22.71–28.77)	23.15±4.82 (18.40–28.42)	0.636
Body surface area (m^2) mean±s.d. (range)	1.69±0.19 (1.50–1.93)	1.61±0.22 (1.38–1.83)	0.528
Renal morphology			
Parenchymal volume (ml) mean±s.d. (range)	82.57±13.40 (68.53–104.21)	88.21±13.50 (51.65–133.41)	0.730
MPT (mm) mean±s.d. (range)	14.60±1.14 (13.33–16.33)	14.13±3.88 (7.67–17.80)	0.802
MCT (mm) mean±s.d. (range)	4.89±1.65 (3.0–7.0)	5.42±2.20 (2.67–8.67)	0.671
MMT (mm) mean±s.d. (range)	9.71±2.43 (7.33–13.33)	8.72±3.22 (5.00–13.63)	0.586
Estimated cortical mass (ml)[a] mean±s.d. (range)	29.17±14.76 (12.59–50.89)	32.45±11.37 (17.96–49.82)	0.686
Parenchymal volume/ isoSK-GFR ratio (ml per ml/min of GFR) mean±s.d. (range)	23.35±6.83[b] (16.64–31.39)	7.61±3.03 (5.11–13.03)	0.001

[a]Estimated cortical mass: (cortical thickness/parenchymal thickness) × parenchymal volume.
[b]*P*=0.001 compared to normal/insignificant and significant RAS groups (see Table 1).

most clinicians use size as measured by bipolar length as one of their guides. Smaller RAS kidneys (generally defined to be less than 8 cm in length) are presumed to have extensive and probable irreversible intra-renal damage, or are thought to contribute little to overall renal function, and so are often not subjected to revascularization procedures. Eleven of the 33 kidneys with significant RAS were defined as small in terms of length; however, a number of these kidneys had a parenchymal volume comparable to that of larger kidneys (greater than 8 cm in length), again suggesting that bipolar length may not be the most appropriate morphological parameter to accurately assess renal size. Six of the 11 small kidneys had isoSK-GFR greater than or equal to 7 ml/min; these kidneys may not normally have been considered for revascularization, but clearly, maintenance of their function by preventing RAO and/or further renal atrophy could be seen as beneficial to limiting the chances of progression to end-stage renal disease in the future. Although decreases in renal length, volume, parenchymal, and cortical thicknesses are usually thought to reflect irreversible intra-renal damage, there is evidence that some of the changes may be reversible so deriving the concept of 'hibernating parenchyma'.[31] Hence, there have been reports of increases in cortical and medullary thicknesses occurring after revascularization of the RAS kidney, suggesting the possibility of some reversibility of parenchymal damage.[32,33] Estimation of the parenchymal volume to isoSK-GFR ratio in kidneys with significant RAS provided support for the concept of 'hibernating parenchyma'. A number of kidneys had a disproportionately greater parenchymal volume: isoSK-GFR raising the possibility that these were kidneys supplied by a hemodynamically significant stenosis, yet without having undergone significant

irreversible renal structural change. This parenchymal volume to isoSK-GFR ratio (or perhaps more accurately cortical volume to isoSK-GFR ratio) has a potential use as a prognostic indicator for revascularization.

This study demonstrates the superiority of 3D over 2D measurements, in predicting isoSK-GFR, and this was particularly noticeable in kidneys supplied by significant RAS. Ultrasound estimations of renal morphology are operator dependent and have been shown to be subject to wide intra- and inter-observer variations;[34] MRI has provided a more accurate means of assessing renal morphology.[20,35,36] Gadolinium-enhanced MRI can provide safe, accurate evaluation of morphology, proximal arterial anatomy, intra-renal hemodynamics, and estimations of single-kidney function in research settings[20,24,35,36] (Buckley DL *et al. Proceedings of the ISMRM 10th Annual Meeting*, 2002; abstract). The future clinical evaluation of ARVD in a one-stop investigation is therefore becoming a real possibility. We acknowledge that there are limitations in our investigative protocol, which involves the use of a 1.0 T scanner with body and spinal coils rather than a volume receiver coil. Nevertheless, we found that the presence of signal intensity degradation was minimal with this protocol and that this did not affect volume analysis using the voxel-count method as all morphological analyses were performed in the coronal plane.

This study demonstrates that the most sensitive morphological markers of both isoSK-GFR and significant RAS are renal 3D volume measurements. The development and progression of renal atrophy is known to occur in kidneys with significant RAS, and the challenge remains to identify those kidneys and intervene at a stage when ischemic changes are still reversible or perhaps before they have even taken place. Approximately 16% of all cases of ARVD are now treated with renal revascularization procedures,[37] and one limitation of the current study is that the predictive value of the MR investigative techniques was not tested in kidneys undergoing renal revascularization. Adding assessment of morphology to that of renal function may hold the key to the appropriate selection of RAS kidneys that are most likely to benefit from revascularization procedures. Further prospective studies will also reveal whether parenchymal volume:SK-GFR analysis can help predict the renal functional response to revascularization, the hypothesis being that kidneys with a disproportionately high parenchymal volume:SK-GFR will be those more likely to manifest improvement.

MATERIALS AND METHODS

Study population

Thirty-five patients with ARVD diagnosed by previous imaging (intra-arterial digital subtraction, MR or CT angiography) were seen consecutively in the renal clinics and consented to participation in the study. The protocol had the approval of the Local Research Ethics Committee. Basic patient demography and subsequent clinical data were recorded. These included age, gender, height, and weight.

Radioisotope single-kidney GFR

The assessment of individual kidney function involved a standard radioisotopic methodology.[26] In this, global GFR was first measured with ^{51}Cr-ethylenediaminetetraacetic acid clearance, and then patients underwent ^{99m}Tc-dimercaptosuccinic acid scintigraphy for the assessment of the differential static radioisotope uptake of each kidney. The individual kidney function was calculated by dividing the global GFR according to the percentage of the uptake of ^{99m}Tc-dimercaptosuccinic acid on scintigraphy. The isoSK-GFR was unadjusted for surface area for correlation analysis with morphological parameters.

Magnetic resonance imaging

MR imaging was performed at 1.0 T (Magnetom Expert; Siemens Medical Systems, Germany) using a combination of quadrature body coil and spine coil for signal reception (no phased-array body coil was available). Data were acquired for both structural and functional analysis (Buckley DL *et al. Proceedings of the ISMRM 10th Annual Meeting 2002*; abstract); only those images subsequently used for the assessment of bipolar length, renal volume, parenchymal, and cortical thickness are detailed below. Following the acquisition of scout images, the following sets of data were all obtained during breath holds. Initially, images were acquired in the coronal plane using a multislice TrueFISP sequence (field of view (FOV) = 380 × 380 mm, 12 slices, slice thickness = 8 mm, gap = 4 mm, matrix = 256 × 256, TR = 7.9 ms, TE = 3.7 ms, flip angle = 80°). Subsequently, 3D volume data were acquired using a FLASH acquisition in the oblique–coronal plane encompassing both kidneys and the descending aorta (TR = 5.4 ms, TE = 2.2 ms, FOV = 350 × 306 × 80 mm, flip angle = 20°, four signal averages, following interpolation in the Fourier domain section thickness = 2.5 mm, matrix = 128 × 112 × 32). Towards the end of the examination, contrast-enhanced MRA (0.175 mmol/kg gadolinium diethylenetriaminepentaacetic acid (Gd-DTPA)) was performed to assess the proximal renal vasculature. Images were again obtained using a 3D-FLASH acquisition in the oblique–coronal plane (TR = 5.7 ms, TE = 2.2 ms, FOV = 400 × 400 × 96 mm, flip angle = 30°, following interpolation in the Fourier domain section thickness = 2 mm, matrix = 256 × 256 × 48). This sequence was repeated to provide images in both the arterial and venous phases of the contrast agent bolus transit.

The renal arterial anatomy was graded as normal vessel, insignificant (<50%) RAS, significant (⩾50%) RAS or complete occlusion (RAO). The kidney volumes were calculated from the 3D volume images using the voxel-count method applied to coronal MR images.[35] In this method, the boundaries of the renal parenchyma of each slice of the kidney were manually mapped. The renal parenchymal volume was then calculated as follows:

$$\text{Renal volume(ml)} = \sum (\text{parenchymal area} \times \text{slice thickness})_{n\,\text{slice}}$$

The 3D-MRA venous phase images were used for bipolar length and cortical thickness analysis. The renal length was measured as the difference between the superior pole and the inferior pole of the kidney. The MPT was calculated from the trueFISP images; the average of three measurements was taken from the superior (SPT), lateral (LPT), and inferior (IPT) aspects of the kidney.[24] Cortical thickness was measured as the width of the high signal intensity peripheral band on the 3D-MRA venous phase images. Three measurements were taken from the superior (SCT), lateral (LCT), and inferior (ICT) poles of the kidney. These were averaged and an

MCT was obtained as follows:

$$\mathrm{MCT\ (mm)} = (\mathrm{SCT} + \mathrm{LCT} + \mathrm{ICT})/3$$

To give an estimate of total cortical mass, the total parenchymal volume was multiplied by the ratio of MCT and MPT (estimated cortical mass (ml)). MMT was calculated as

$$\mathrm{MMT\ (mm)} = ((\mathrm{SPT} + \mathrm{LPT} + \mathrm{IPT})/3) - (\mathrm{SCT} + \mathrm{LCT} + \mathrm{ICT})/3)$$

We have previously assessed the reproducibility and agreement of these measurements of structural parameters. The agreement of volume and cortical thickness measurements were $R^2 = 0.96$ and 0.80, respectively.

Body mass index was calculated from weight and height (weight (kg)/height^2 (m^2)). Body surface area was calculated using the Haycock formula as follows:[38]

$$\mathrm{Body\ surface\ area\ (m^2)} = 0.024265 \times \mathrm{height\ (cm)}^{0.3964} \times \mathrm{weight(kg)}^{0.5378}$$

Evaluation criteria and statistical analysis

Kidneys supplied by completely occluded renal arteries were excluded for correlation analysis between renal morphological parameters and isoSK-GFR as it was assumed that their isoSK-GFR would be negligible. Correlation subanalyses were performed on kidneys with normal vessel or insignificant RAS and compared with kidneys supplied by significant RAS so as to determine whether the isoSK-GFR might be disproportionately low because of a hemodynamically significant stenosis. Pearson's correlation coefficient was used to test the relationships between renal length, volume, parenchymal thickness, cortical thickness, and isoSK-GFR. Parametric data are presented as mean $\pm$ standard deviation and grouped according to severity of arterial stenosis, and renal morphology. Differences in morphological parameters and isoSK-GFR between groups were compared by the use of analysis of variance and *post hoc* analysis using Bonferroni correction. Significance level was set at 5%. SPSS software was used for all statistical analysis.

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