A clinical MRI investigation of the relationship between kidney volume measurements and renal function in patients with renovascular disease

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ABSTRACT. Recent improvements in MR image acquisition and post-processing techniques have allowed quantitative kidney volume measurements to be derived from patient studies. These morphological indices can provide ''snapshot'' assessments that may be related to kidney function. The study objective was to measure cortical and total kidney volumes in patients with renovascular disease (RVD) using contrast-enhanced MR angiography (CE-MRA) in order to assess the reproducibility of the technique and to investigate associations between volumes and renal function as measured by glomerular filtration rate (GFR) calculations. 50 patients with RVD were scanned using CE-MRA. Kidney lengths, volumes and renal artery stenoses (RAS) were evaluated, and GFR was calculated using clinical formulae and nuclear medicine isotope renography. Mean MRI kidney lengths were 10.3 ± 0.2 cm, and mean MRI volumes were 74.9 ± 3.6 cm^3 (cortical) and 128.5 ± 5.3 cm^3 (total). Kidneys supplied by moderately stenosed arteries had enlarged lengths and volumes, whilst those supplied by severely stenosed arteries had significantly smaller lengths ($p<0.001$) and volumes ($p<0.001$). There was a clear association between MRI cortical volume and GFR ($r=0.74$, $p<0.001$, $n=48$), but less so between kidney length and GFR ($r=0.54$, $p<0.001$, $n=48$). For individual patients, left/right cortical volume differences were small provided that severe RAS was not present, but large left/right volume differences and a GFR reduction were noted when severe RAS was present. The cortical volume distribution provides a useful single-timepoint indication of kidney function as defined by GFR, with no additional data acquisition required other than that of standard CE-MRA examination.

Contrast enhanced MR angiography (CE-MRA) is an established MRI technique that can provide clear images of the renal architecture and vasculature [1, 2]. It is possible to identify the severity of renal artery stenoses (RAS) in patients who display clinical symptoms of hypertension or suspected renal impairment [3, 4], and the method provides a useful alternative to ultrasound or catheter angiography [5–8]. However, in addition to RAS measurements, it is also possible to extract quantitative indices of renal morphology (such as renal length and cortical or total kidney volumes) from CE-MRA data using appropriate post-processing [6, 9–12].

Cortical volume MRI measurements have previously been reported in human studies [12–14], and also in *in vitro* studies of porcine kidneys [15]. Volumes can be calculated from voxel counting, a technique where areas of high-signal renal cortex are extracted from the rest of the kidney using simple post-processing software. Images can be analysed on a slice-by-slice basis, and volumes can be calculated by multiplying the sum cortical area on each slice by the image slice thickness (Simpson's rule). Total

kidney volumes can also be calculated by including areas of medulla in addition to the renal cortex.

Intervention by renal angioplasty or stent placement in patients with RAS is thought to be most appropriate in kidneys where it is possible to identify deteriorating renal function [16]. MRI methods such as contrast enhanced MR renography (CE-MRR) for exploring renal cortical perfusion and function are in the stages of development and show early promise [17–23], but the widely accepted standard index for measurement of kidney function is glomerular filtration rate (GFR) [24]. It is believed that intervention may be more successful in halting the progression (or maximizing the potential for reversible ischaemic change) of renal impairment in cases of haemodynamically significant renovascular disease (RVD) where the functioning renal morphology, or mass, is maintained. MRI measurement of cortical and total kidney volumes has the potential to quantify functioning renal mass, which has traditionally been characterized by simple measurements of kidney length.

The aim of the study was to measure cortical and total kidney volumes using MRI, together with pole-to-pole kidney lengths, in a cohort of patients with suspected RVD, and to explore the relationship between these morphological indices with MRI severity of renal artery stenoses (RAS) and clinical renal function measurements of GFR.

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Patients, methods and materials

The study was undertaken after Regional Ethics Committee approval had been obtained. 50 fully informed and consenting patient volunteers (25 males and 25 females, age range 34–89 years, mean 66 years) with clinical hypertension and/or suspicion of impaired renal function were recruited for CE-MRA. A total of 99 kidneys were evaluated.

MRI

MRI was performed on a 1.5 T Symphony system (Siemens Medical, Erlangen, Germany) using a phased array body coil. CE-MRA data were acquired in a coronal oblique plane (along the length of the descending aorta) prior to delivery of contrast agent using a fat-suppressed 3D fast low-angle shot (FLASH) sequence with imaging parameters repetition time (TR)/echo time (TE) 4.6 ms/1.8 ms and 25° flip angle. A volume series of 56 contiguous coronal oblique slices (each 1.29–1.57 mm thick) was acquired whilst the patient held their breath at end inspiration. This slice coverage was sufficient to include both kidneys and renal arteries. The image matrix was 180×384 pixels, covering a rectangular (6/8) field of view ranging from 360 mm to 420 mm (dependent upon the size of the patient). The acquired phase resolution was 62.5% with the remainder of the phase encode steps being zero-filled. Interpolation was also utilized to enable the images to be visualized on a 512 matrix.

Following acquisition of the pre-contrast MRI dataset, a suitable bolus timing delay (required to allow the contrast agent sufficient time to travel from the point of injection to the aorta at the level of the renal arteries) was derived from a ''test bolus'' timing sequence. Subsequently, a 20 ml bolus of contrast agent (Gadoteridol Prohance™; Bracco, Italy) followed by a 20 ml saline flush was delivered into a vein in the antecubital fossa using a spectris II infusion pump injector (Medrad, Philadelphia, PA), and post-contrast (arterial and early venous phase) MRI datasets were acquired. Subtraction of the pre-contrast dataset from the arterial phase post-contrast dataset was also performed, and maximum intensity projection (MIP) images were derived from the resulting subtraction images.

Quality assurance (''Eurospin'') test phantom experiments were also undertaken to ensure that the MRI slice thickness and resolution was within specification for the MRI system used.

Renal artery stenosis assessments

RAS measurements were derived from careful examination of the resulting arterial phase source images and the MIP data. Stenoses were assessed by a Consultant Radiologist (JGH), who identified the percentage obstruction of each arterial lumen as ''minimal'' (category 1, 0–30%), ''moderate'' (category 2, 31–70%) or ''severe'' (category 3, 71–100%). The rationale for this categorisation was that a minimal <30% stenosis was considered to represent an artery with little or no significant haemodynamic obstruction, whilst a severe >70% stenosis was considered to represent an artery with a severe haemodynamic obstruction by established clinical criteria. Arteries with stenoses above 30% but less than 70% were categorised as ''moderate'', with the acknowledgment that this category may have contained haemodynamically normal and abnormal examples. It is well established that assessment of RAS is to a certain extent subjective, and that overestimation of the degree of RAS is possible using MRI relative to the gold standard of catheter angiography. However, it was elected not to undertake qualitative RAS reproducibility assessments or to perform comparison testing between MRI and catheter angiography because this information is extensively documented elsewhere [7, 25–27]. Accessory vessels were noted if present, but not analysed further since the principal vessel was considered to contribute primarily to the haemodynamic status of the kidney.

The RAS severity was also recorded on a ''per patient'' basis by considering both left and right arteries together. Arteries were defined as having bilaterally minimal disease if the stenosis scoring was recorded as 1,2 or 2,1, and bilaterally severe disease if the stenosis scoring was recorded as 2,3 or 3,2. Other combinations of stenosis pattern (1,3 3,1 or 2,2) were categorised as ''moderate'' on the basis that the average degree of renal function impairment was likely to be neither bilaterally minimal nor severe. Again, it was accepted that this group would probably contain both functionally normal and abnormal examples.

Kidney volume and length assessments

Individual kidney volumes were calculated from the second post-contrast (early venous phase) MRA datasets. Segmentation of kidney cortex was performed on a Siemens Virtuoso workstation by using the voxel count method, incorporating regions of hyperintense cortical signal on a slice-by-slice basis (Figure 1) after defining a suitable signal intensity threshold and window. It was possible to selectively edit the ROI by manually using ''add'' or ''cut'' tools as appropriate, and this process was repeated for all image slices across the kidney. Segmentation of total volumes (to include cortical and medullary tissue) was performed in a similar manner. Generation of both cortical and total volumes for each kidney took approximately 10–15 min per kidney, but additional time was periodically required if the kidney under examination was severely diseased. Cortical and total volumes were normalized with respect to body surface area (BSA) [28] for each patient, and recorded together with the original non-normalized measurements. Combined kidney volumes (sum of left and right volume) were also calculated for each pair of kidneys, and right/left volume differences were also recorded for each pair of kidneys. One observer (SJG) carried out the full segmentation process, with another observer (KA) repeating the measurements on a subset of 54 of the kidneys (18 each with minimal, moderate and severe RAS) to allow both intraobserver and interobserver coefficients of variation (CoV) to be ascertained.

An example of a patient with moderate and severe RAS, together with cortical volume segmentations is highlighted in Figure 1.
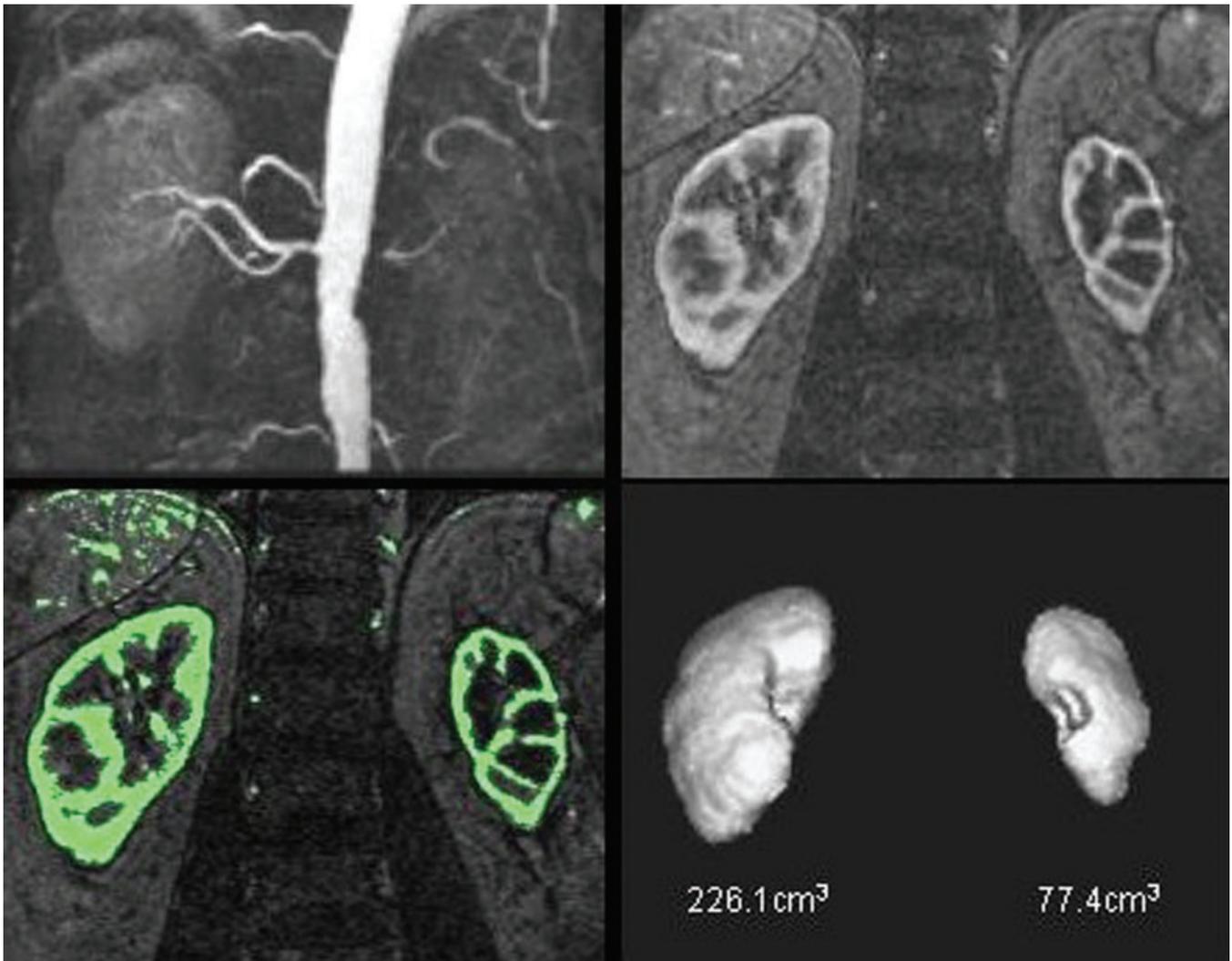
Figure 1. (a) A maximum intensity projection (MIP) image highlighting moderate (category 2, 31-70%) right renal artery stenosis (RAS) and severe (category 3, 71-100%) left RAS, together with (b) a representative central slice of a post-contrast (early venous phase) dataset. (c) The signal intensity threshold technique and associated region of interest (ROI) selection is illustrated, where the cortical volume is calculated using pixel counting. (d) The final reconstructed volume is highlighted, where the right kidney is relatively enlarged (226.1 cm³) and the left kidney is relatively small (77.4 cm³).

In addition to volume analysis, maximum pole-to-pole kidney lengths were carefully recorded for each kidney using multiplanar reconstruction (MPR) measurement software (Numaris 3.1; Siemens, Erlangen, Germany). Kidney lengths were normalized with respect to body surface area (BSA) for each patient, and recorded together with the non-normalized assessments. Combined kidney length measurements (sum of left and right lengths) were also calculated, and right/left length differences were also recorded for each pair of kidneys.

Glomerular filtration rate assessments

Clinical evaluation of creatinine clearance was calculated for each patient using the Cockroft-Gault formula (Cockroft-Gault glomerular filtration rate, CG-GFR) [29], and an estimated Modification of Diet in Renal Disease, GFR (MDRD-GFR) was also calculated using clinical parameters defined in the MDRD study [29]. For calculation of CG-GFR, patient age, sex, weight and serum creatinine concentration were all recorded, and for calculation of MDRD-GFR the same variables were recorded along with serum albumin concentration and serum urea nitrogen concentration. These values are detailed in the patient demographic information (Table 1).

A subset of the patients also underwent a nuclear medicine GFR (NM-GFR) examination prior to MRI as part of their routine clinical diagnostic procedure. The NM-GFR information was derived from ^{99}Tc^m–DTPA or ^{51}Cr–EDTA investigations. Where possible (see exclusion criteria) these data were compared with MRI measurements of cortical/total volumes and pole-to-pole lengths, and also with the CG-GFR and MDRD-GFR formulae.

Statistical methods

Patient demographics detailing the clinical measurements recorded in this study are highlighted in Table 1.

Table 1. Patient demographic information

	Mean	Range
Patients		
Number of males	25	–
Number of females	25	–
Age ranges		
Males (years)	66	38–89
Females (years)	66	34–81
Physical characteristics		
Height (m)	1.66	1.52–1.85
Weight (kg)	76	51–128
BMI	27.7	19.5–37.4
Blood pressure		
Systolic blood pressure (mm Hg)	151	100–210
Diastolic blood pressure (mm Hg)	80	58–130
Serum variables		
Serum creatinine (mg dl^{-1})	144	68–361
Serum albumin (g dl^{-1})	41	33–46
Serum urea nitrogen (mg dl^{-1})	10	3.1–27.2
MRI RAS scoring		
Bilateral minimal (1,1)	$n=18$	–
Bilateral moderate (2,2)	$n=1$	–
Bilateral severe (3,3)	$n=5$	–
None–moderate (2,0 or 0,2)	$n=1$	–
Minimal–moderate (1,2 or 2,1)	$n=5$	–
Minimal–severe (1,3 or 3,1)	$n=10$	–
Moderate–severe (2,3 or 3,2)	$n=10$	–

BMI, body mass index; RAS, renal artery stenosis.

The cortical and total MRI volume reproducibility was evaluated by calculating test–retest coefficients of variation for intraobserver and interobserver measurements. Quantitative kidney volumes and pole-to-pole length measurements were compared for patients with varying degrees of RAS, and one-way analysis of variance (ANOVA) with post-hoc analysis was performed to examine the null hypotheses that no cortical volume, total volume, or length differences would exist between the data when stratified by degree of RAS. Correlation coefficients were also observed for inter-relationships between kidney volumes, pole-to-pole lengths and GFR measurements. Finally, left/right kidney volume and pole-to-pole length differences were compared with GFR measurements for patients with differing degrees of bilateral RAS. All statistical testing was carried out using statistics package SPSS (version 11.5; SPSS Inc., Chicago, IL).

Patient exclusion criteria

Of the 50 patients included in the study, scoring of RAS severity and measurement of cortical/total kidney volumes and pole-to-pole lengths was successfully completed for all patients, and clinical measurements of CG-GFR and MDRD-GFR were obtained for 48 patients. Nuclear medicine examinations were not carried out on all patients in the study because they were not deemed clinically necessary for all individuals. The nuclear medicine scans were undertaken as part of routine clinical procedure such that the timescale between nuclear medicine and MRI examinations was variable. It was possible to compare MRI and nuclear medicine data in 30 patients, with a mean delay between nuclear medicine and MRI examinations of approximately 3 months.

Results

Reproducibility study

For kidney volume reproducibility measurements, CoVs ranged from 2.1% (intraobserver, total volume, moderate RAS patients) to 6.7% (interobserver, cortical volume, severe RAS patients). All volume reproducibility measurements are fully detailed in Table 2. Reproducibility of pole-to-pole length measurements was not assessed since the measurement was comparatively simple to undertake.

RAS assessments – individual kidneys

A full breakdown of the RAS scoring is detailed in the patient demographic information (Table 1), and an example of a patient with right moderate RAS and left severe RAS, together with associated segmented volumes is illustrated and described in Figure 1. In addition to the tabulated RAS scoring, 17 accessory vessels were noted in 14 of the patients (3 of the patients had accessory vessels supplying both left and right kidneys).

Volume and length assessments – individual kidneys

Cortical volumes ranged from 4.5 cm^3 to 153.3 cm^3 (mean 74.9$\pm$3.6 cm^3) and total volumes ranged from 22.0 cm^3 to 252.8 cm^3 (mean 128.5$\pm$5.3 cm^3) across the cohort. When the patient data were subdivided by RAS category (Figure 2), the mean cortical kidney volume for the group with severe RAS (53.3$\pm$6.2 cm^3) was significantly lower than for those with minimal or moderate

Table 2. Reproducibility data for patient MRI kidney volumes

Kidney description	Intraobserver Cortical Vol.	Intraobserver Total Vol.	Interobserver Cortical Vol.	Interobserver Total Vol.
	CoV (%)	CoV (%)	CoV (%)	CoV (%)
All kidneys	4.2	2.9	6.1	4.3
Minimal RAS	3.9	2.3	6.1	2.9
Moderate RAS	5.0	2.1	5.6	3.9
Severe RAS	3.7	4.1	6.7	6.1

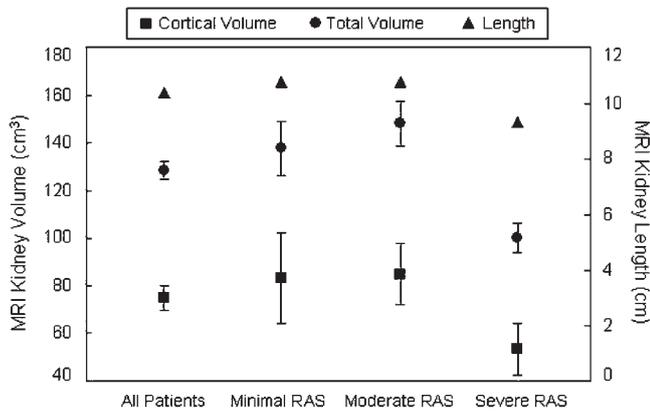RAS, renal artery stenosis; CoV, coefficient of variation.

Figure 2. Mean kidney lengths and cortical/total kidney volumes, as subdivided by renal artery stenosis (RAS) category. The mean kidney volumes were reduced by 37% (cortical) and 32% (total) between those patients with moderate RAS and those with severe RAS, whereas the mean kidney length was only reduced by 14%.

RAS (83.4 ± 11.7 cm^3 and 84.9 ± 9.4 cm^3, respectively; $p<0.001$). A similar pattern was also observed for total kidney volumes ($p<0.001$). Normalization of volumes with respect to BSA demonstrated no change of pattern to the volume distribution or statistical significance.

Kidney lengths varied from 5.4 cm to 13.9 cm (mean 10.3 ± 0.2 cm) across the cohort. Again, when the patient data were subdivided by degree of RAS category, the mean kidney length for patients with severe RAS (9.3 ± 0.4 cm) was significantly smaller than for those with minimal (10.8 ± 0.2 cm) or moderate RAS (10.8 ± 0.3 cm) ($p<0.001$ for both cases). Again, normalization of kidney lengths with respect to BSA had no effect on the pattern or statistical significance of the outcome.

Combined kidney GFR assessments

The mean GFR values obtained using each technique are detailed in Table 3. The mean CG-GFR and NM-GFR measurements were broadly similar for all patients and subgroups, but the MDRD-GFR was consistently smaller, except for the case of severe RAS. For all patients, GFR measurements ranged from 14.5 ml min^{-1} to 141.3 ml min^{-1} (CG-GFR), 10.9 ml min^{-1} to 100.5 ml min^{-1} (MDRD-GFR) and 14.3 ml min^{-1} to 121.2 ml min^{-1} (NM-GFR). As expected, the mean GFR values for each technique demonstrated a drop as the severity of RAS supplying the kidneys increased.

Correlation of combined kidney volumes and combined lengths with GFR parameters

When the sum of each left and right kidney volume (per patient) was compared with the global GFR parameters, combined cortical volumes (Figure 3) and combined total volumes were strongly correlated with CG-GFR and NM-GFR measurements, but weakly correlated with MDRD-GFR values (Table 4). Correlations of combined pole-to-pole kidney lengths with CG-GFR, NM-GFR and MDRD-GFR values followed a similar but marginally weaker pattern to those obtained for volumes. Combined cortical volumes normalized to BSA were also correlated with GFR measurements, but the normalized values resulted in a marginally worse Pearson correlation coefficient in most cases.

When the combined volume data were stratified by degree of right/left RAS, the clearest correlations were those observed between the combined cortical volumes and the GFR parameters. The best case Pearson correlation coefficient between combined cortical volume and CG-GFR was obtained for patients with severe RAS (either 2,3; 3,2; or 3,3 stenosis gradings, $r=0.94$, $p<0.001$). A good association was also evident between combined cortical volume and CG-GFR for patients with minimal RAS (either 1,1; 2,1; or 1,2 stenosis gradings, $r=0.79$, $p<0.001$). However, the relationship between combined cortical volume and CG-GFR for those patients with moderate RAS (either 2,2; 1,3; or 3,1) was less clear ($r=0.32$), possibly reflecting the heterogeneity of disease conditions that were likely to be present in this subgroup. The association between combined cortical volumes and NM-GFR yielded correlation coefficients of $r=0.85$ ($p<0.001$), $r=0.66$ ($p<0.05$) and $r=0.61$ ($p<0.05$) for those patients with combined minimal, moderate and severe RAS, respectively.

Correlation of left/right kidney volume and length differences with GFR parameters

Finally, a graph of left/right cortical kidney volume differences was plotted for different degrees of left/right RAS severity (Figure 4). In this patient cohort, the left and right cortical volumes remained similar, provided that the artery supplying either kidney was no more than moderately stenosed. However, when severe RAS was observed in the supplying artery of either kidney, left/right kidney volume differences became very apparent. This was most pronounced for the moderate-severe (RAS 2,3) subgroup where the mean difference in kidney volumes was 58 cm^3 (corresponding to a mean

Table 3. Clinical indices of creatinine clearance and GFR as stratified by degree of RAS

Patient cohort stratification	CG-GFR (ml min^{-1})	MDRD-GFR (ml min^{-1})	NM-GFR (ml min^{-1})
All patients	52.6 ± 3.9	45.0 ± 3.0	53.5 ± 4.8
Minimal RAS (1,1; 1,2; or 2,1)	58.2 ± 6.2	45.5 ± 5.0	62.3 ± 9.4
Moderate RAS (1,3; 3,1; or 2,2)	56.8 ± 7.5	47.0 ± 5.2	55.0 ± 13.1
Severe RAS (2,3; 3,2; or 3,3)	41.2 ± 6.2	42.7 ± 5.1	41.0 ± 5.3

GFR, glomerular filtration rate; RAS, renal artery stenosis; CG, Cockroft-Gault creatinine clearance; MDRD, Modification of Diet in Renal Disease; NM, nuclear medicine.
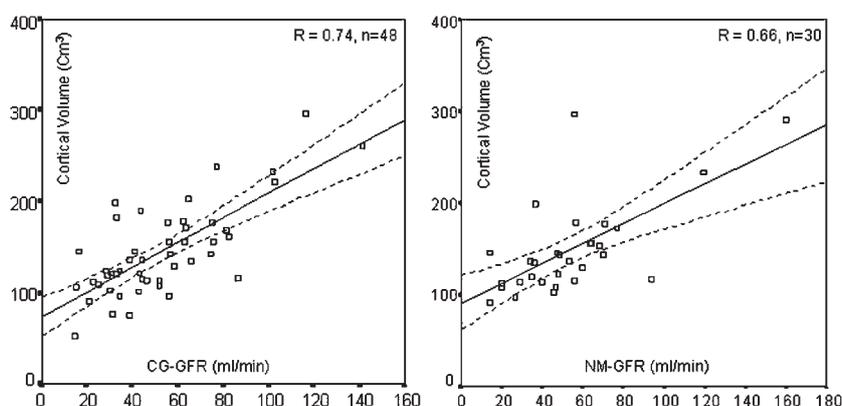
Figure 3. Correlation of combined cortical volumes with (i) CG-GFR values and (ii) NM-GFR values for individual patients.

ipsilateral-contralateral cortical volume difference of 57.4%). Kidney length measurements followed a similar, but less well-defined pattern (mean ipsilateral-contralateral length difference 24.3%). The corresponding mean NM-GFRs remained relatively normal whilst the artery supplying the contralateral kidney was only minimally stenosed, but began to fall when the arteries were moderately or severely stenosed.

Discussion

In this study we have investigated the association between kidney volume and pole-to-pole length measurements (morphological indices) and glomerular filtration rates (functional indices) in patients with varying degrees of renal artery stenosis. The relationship between renal volume and function appears to be fairly complex. We have observed the previously reported phenomenon of compensatory enlargement in contralateral kidney mass in response to loss of mass in the ipsilateral kidney [11]. In our study, this finding was noted across the patient cohort, and also commonly on a per patient basis for those with ipsilateral severe and contralateral moderate RAS. It is believed that the relative cortical volumes of each kidney can assist with clinical decision-making when renal artery interventional procedures are to be considered before significant renal impairment has occurred. This would appear to be particularly appropriate in cases of moderate–severe or bilateral severe stenosis, but may also be appropriate where ipsilateral arteries are significantly stenosed and are coupled with non-stenosed contralateral arteries (patient category 1,3 in Figure 4). We hypothesise that in these cases the relative changes to the functioning cortical volumes appear to highlight differences that

have yet to become apparent as a notable change to the GFR, and intervention at this stage may help to preserve the combined renal function. However, we acknowledge that these findings would need to be investigated further as part of a larger formal renal intervention and MRI study.

We elected not to compare MRI measurements of RAS against the gold standard of catheter angiography. Previous studies have identified such intermodality comparisons with the consensus that whilst MRI is prone to small systematic overestimation of RAS, it does provide a safe, non-invasive and reliable method of characterizing RAS severity [30].

The voxel count method that we employed to measure the kidney volumes was tested for intraobserver and interobserver variation (CoV), and found to be reproducible. The test–retest CoV for total kidney volumes was generally less than for cortical volumes, and the CoVs were found to generally increase as the severity of RAS increased. This follows, since it is more difficult to discriminate between cortical and medullary tissue in cases where the kidney has begun to show evidence of ischaemic tissue loss. However, the CoVs are sufficiently small to suggest that longitudinal monitoring of kidney volume changes may be possible using this technique, particularly if the same segmenter is used for acquiring the measurements at each timepoint.

The total kidney volumes reported in this paper (22.0–252.8 cm^3) extend over a similar range to that recently reported [12] for patients with diagnosed atherosclerotic RVD, as confirmed by previous imaging (parenchymal volumes 17.3–337.09 ml). The inclusion criteria for our study were less stringent, although they enabled us to invoke a ''normal clinical practice'' model in order to identify the status of patient referrals for CE-MRA at our institution over the course of the investigation. The

Table 4. Pearson correlation coefficients obtained for renal volume, length and GFR comparisons (* = $p<0.001$)

	Total volume	Kidney length	CG-GFR	MDRD-GFR	NM-GFR
Cortical volume	0.85*	0.69*	0.74*	0.02	0.66*
Total volume	–	0.78*	0.69*	0.03	0.61*
Kidney length	–	–	0.54*	−0.05	0.56*
CG-GFR	–	–	–	0.08	0.79*
MDRD-GFR	–	–	–	–	0.15
NM-GFR	–	–	–	–	–

GFR, glomerular filtration rate; CG, Cockroft-Gault creatinine clearance; MDRD, Modification of Diet in Renal Disease; NM, nuclear medicine.
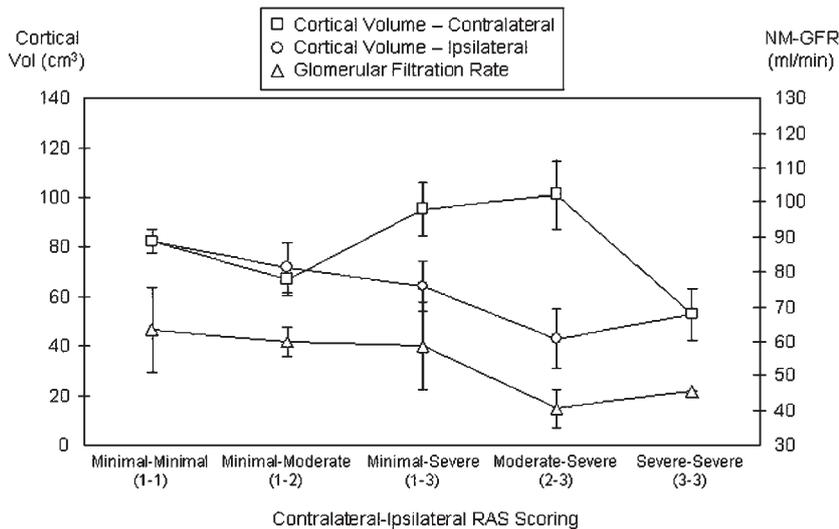
Figure 4. Variation of contralateral and ipsilateral cortical volumes with glomerular filtration rate for kidneys with differing degrees of renal artery stenosis.

overlap of the volumetric data between our study and that reported by Cheung et al [12] suggests that our patient cohorts are probably similar despite the differences in inclusion criteria, and truly representative of the typical kidney volume distribution for patients with RVD.

When the volume data were stratified by degree of RAS, large volume kidneys that were supplied by moderately stenosed arteries were repeatedly associated with much smaller volume contralateral kidneys, which were supplied by severely stenosed arteries. As previously discussed, these data may demonstrate evidence of preservation of kidney function via this compensatory mechanism. It would be interesting to obtain correlative measures of the split renal function in these patients via nuclear medicine studies in order to further validate this evidence.

In this study, normalization of kidney volumes and lengths were calculated with respect to the BSA for each patient. However, this had little or no effect on the outcome of the data as stratified by degree of RAS, and in the case of GFR comparisons actually made the correlations slightly worse. The reason for this is unknown, although similar findings have been reported when data have been normalized with respect to vertebral body height [31].

The MRI sequences in this study were optimized to ensure that images were acquired contiguously and using thin sections. Whereas in the past, slice thickness values ranging from 2 mm to 8 mm have been reported in other studies, our section thickness of 1.35 mm is, to our knowledge, the thinnest slice resolution applied to volumetric assessment of the kidneys. Whilst this results in the acquisition of many extra slices and therefore increases the image post processing workload, it minimizes problems associated with partial volume errors.

By acquiring early venous phase data it was possible to obtain cortical kidney volumes as well as total volumes. However, the contrast agent is most likely to be taken up by the entire glomerular tubular structure, which extends into the medullary region of the kidney. It may therefore be more appropriate to describe the portion of enhancing kidney at this stage as a glomerular tubular (or GT) volume, rather than a cortical volume.

Our method of acquiring early venous phase data was not tested for reproducibility, since it was not appropriate to subject each patient to a double dose of contrast agent and repeated scans. However, since the onset of the imaging sequence is governed by careful bolus timing, it is anticipated that the cortical (GT) volume is comparable and reproducible between different patients and examinations.

It was interesting to note that the correlation of kidney length versus cortical volume was found to be worse than the correlation of kidney length versus total kidney volume. The cortical volume is thought to represent a truer measure of functioning renal tissue than total volume, since it omits the volume associated with the deep medullary tissue and the collecting system. Furthermore, combined cortical volume was better correlated with GFR in this cohort relative to renal length versus GFR, and ipsilateral/contralateral cortical volume variations with GFR were far easier to detect than corresponding kidney length variations with GFR. This, along with the increased sensitivity of kidney volume changes in relation to RAS severity (Figures 2 and 4), casts doubt as to the validity of using kidney length as an assessment measure in patients with RVD.

Two of the different methods of GFR measurement (CG-GFR and NM-GFR) showed broad agreement across the patient cohort. However, MDRD-GFR measurements were notably lower, particularly for patients where the degree of RAS was also low, as recently observed by Rule et al [32].

In this paper we have considered the correlation of combined kidney volumes with clinical measures of GFR for patients with varying degrees of RAS. However, it should be recognized that renal impairment may not necessarily be due to RAS alone, as other factors such as pyelonephritis, nephritis or small vessel disease, *e.g.* diabetes mellitus may predominate. In these situations it may be that a lack of correlation between renal cortical and measured GFR would be observed, although this has not been considered in this study.

In conclusion, we have reported the relationship between kidney volumes, lengths, GFR measurements, and severity of RAS in patients with renovascular disease. MRI cortical volumes are able to provide a

reproducible clinical measure of the extent of functional tissue loss in patients with RVD, and can be derived from a standard CE-MRA examination. Careful monitoring of relative renal cortical volumes together with RAS scoring may offer suitable MRI endpoints by which to evaluate future longitudinal studies designed to aid the selection of patients with RVD who may benefit most from interventional procedures.

Acknowledgments

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