BOLD changes after revascularization in renal artery stenosis patients - preliminary results

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Atheromatous renovascular disease (ARVD) is a commonly encountered yet challenging disease to manage. Renal artery stenosis (RAS) is usually focal and is of great clinical importance, not only due to the potential blood flow-limiting effects upon the renal circulation (and subsequent intra-renal ischaemia), but also downstream neuro-hormonal and cytokine release resulting in hypertension, renal impairment and fluid and salt retention. About 90% of RAS lesions are 'ostial', occurring unilaterally or bilaterally within 1 cm of the origin of the renal artery and can be treated with renal revascularization. However, renal functional outcomes after revascularization in ARVD are unpredictable with only 30% of patients expected to improve. Prediction of beneficial response remains a great challenge, and is especially important given the small but significant risks of stenting[1].

Blood oxygen level dependent (BOLD) imaging is an MRI technique that does not require contrast administration, and indirectly detects changes in intra-renal oxygenation. R2* values correlate positively with tissue oxygen metabolism and changes in the renal BOLD response could be demonstrated following iv administration of Frusemide in human and pig renal impairment models[2,3].

AIMS:

The aim of the current study was to investigate renal parenchymal BOLD response to renal artery revascularization in patients with severe renal artery stenosis and correlate imaging findings with changes in single-kidney glomerular filtration rate (as measured by radioisotope techniques).

STUDY DESIGN:

Patients presenting to our tertiary nephrology referral centre who were deemed suitable for renal revascularization were approached for recruitment into this prospective study. The decision for revascularization was made on clinical grounds, such as poorly controlled hypertension on 6 or more anti-hypertensive agents, deteriorating renal function or flash pulmonary oedema. Age and co-morbidity matched controls were also recruited into the trial. The renovascular patients underwent BOLD-MRI before and after renal artery revascularization, while the control group was imaged only at baseline. Both patients and controls had a radioisotope single kidney GFR measurement (before and after revascularization in the patient group, only on one occasion in the control group). A total of 18 patients (11 males, 7 females, mean age 66.4 ± 9.7, range 50 – 82 years) and 10 controls (6 males, 4 females, mean age 56.9 ± 13.3, range 39-81 years) were recruited. Full ethical approval from the local and regional ethical committees was sought and informed consent obtained from all participants.

METHODS:

All MRI data was collected on a Philips 3T Achieva MR scanner using a 2D gradient echo breath-hold acquisition and 2 echo times (TE_1 = 1.9 ms and TE_2 = 25 ms). Ten coronal-oblique slices covering both kidneys were acquired. Other MR parameters were: FOV = 400 x 400 mm, 128 x 90 matrix, slice thickness = 8 mm, flip angle = 60 degrees, TR = 271. The raw MRI data was transferred to a dedicated workstation and T2* and R2* (= 1/T2*) were calculated by a 2-parameter fit using a dedicated software package (Apollo Medical Imaging Technology, Melbourne, Australia). Parenchymal regions of interest (ROIs) were defined on a representative slice through the middle of each kidney and mean R2* values calculated.

SK-GFR was calculated using radioisotope techniques with ^{51}Cr-Ethylenediaminetetraacetic acid (^{51}Cr-EDTA) clearance and ^{99m}Tc-dimercaptosuccinic acid (^{99m}Tc-DMSA) scintigraphy for the assessment of the differential radioisotope uptake of each kidney. This was performed at baseline and at 4 months after revascularization in the renovascular patients, and only at baseline in the control patients. Improvement in renal function was regarded as >15% or >1ml/min change in an individual kidney.

A total of 23 stented kidneys and 24 control kidneys could be analyzed). Statistical analyses

	Improved N = 8	Stable N = 10	Deteriorated N = 5	Controls N = 24	P
Baseline SK-GFR (ml/min)	13.74 (12.12), 3.61 - 23.88	23.39 (13.74), 13.56 - 33.21	19.69 (11.64), 5.24 - 34.15	25.74 (14.71), 19.53 - 31.95	0.217
R2* (s^{-1})	28.41 (4.48), 24.67 - 32.16	27.75 (3.89), 26.97 - 30.53	27.44 (3.68), 22.87 - 32.00	25.89 (2.79), 24.71 - 37.07	0.029
R2* / SK-GFR	5.91 (6.52), 0.46 – 13.54	1.78 (1.11), 0.98 – 2.57	2.15 (1.79), -0.06 – 4.37	1.40 (0.91), 1.02 – 1.78	0.003

Table 1. Individual renal response of stented kidneys assessed by isoSK-GFR and mean R2. Results are presented as Mean (Standard Deviation), (95% confidence interval).*

were performed using SPSS version 15.0. Continuous data following a normal distribution was described in terms of the mean and standard deviation. Discrete data was described as number and percentage of the grouping. Pre- and post- revascularization results were evaluated using Student's t-test. ANOVA with Bonferroni correction was used to compare T2* and R2* data between groups (kidneys that improved > 15%, kidneys that remained stable between -15% - 15% and kidneys that deteriorated >-15% of baseline SK-GFR). T2* to SK-GFR and R2* to GFR ratios were also calculated and compared between the groups. All statistical analyses performed were considered significant at a level of $p < 0.05$.

RESULTS:

The results are summarized in **Table 1**. There were no significant differences regarding baseline SK-GFR between the kidneys that improved, remained stable, deteriorated or controls. R2* values were significantly higher (p = 0.029) in kidneys whose renal function subsequently improved (28.41 s^{-1}) vs. those who stayed stable (27.75 s^{-1}), deteriorated (27.44 s^{-1}) or control kidneys (25.89 s^{-1}). In addition, the ratio of R2* to SK-GFR was significantly greater in improver kidneys (p = 0.003).

CONCLUSION:

These early results show that BOLD imaging, presumably by detecting intra-renal hypoxia in still viable renal parenchyma, may be a valuable addition to the current standard investigative protocol for ARVD. BOLD imaging is non-invasive, quick to perform (one breathhold) and could provide guidance on the likelihood of kidneys responding to revascularization alongside measures of SK-GFR.

References: 1. Bax L, J Nephrol 16:807-812, 2003; 2. Djamali A, Am J Physiol Renal Physiol 292:F513-F522, 200; 3. Textor SC, J Am Soc Nephrol 19;