Non-Invasive Investigation of Diabetic Kidney Disease by Magnetic Resonance Imaging

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Introduction

We have applied MR imaging methods to diabetic kidney disease with the aim of assessing structural and functional changes in very early kidney disease. Chronic kidney disease is common and over 6000 individuals commence renal replacement therapy in the UK annually, of which ~20% have diabetes. Early diabetic nephropathy is characterised by glomerular hyperfiltration and microalbuminuria, abnormal blood flow and disruption of normal interplay between cortex and medulla (1). The renal medulla is particularly sensitive to hypoxia. Hyperglycaemia, decreased nitric oxide availability and increased oxidative stress may all contribute to increased oxygen consumption. MRI allows non-invasive measurement of both structural information about the renal parenchyma and vessels, and functional information such as perfusion, filtration and oxygenation (2). We have investigated the differences in kidney structure, blood flow and oxygenation between volunteers with Type 1 diabetes (T1D) with and without diabetic nephropathy, and in non-diabetic control subjects. For this pilot study we hypothesised that early changes in kidney structure and function caused by diabetic nephropathy could be identified by altered renal structure, blood flow, and changes in oxygenation on water loading. Reports have suggested that water-loading-induced increases in medullary blood perfusion and oxygenation observed in normal kidneys may not occur in diabetic subjects, leading to hypoxia and ensuing cumulative tissue damage (3).

Methods

Study volunteers comprised three age- and sex-matched groups: longstanding T1D patients with persistently normal albumin excretion and duration of diabetes > 15 years (ie. low risk of nephropathy, n=7), longstanding T1D patients with persistent microalbuminuria but estimated glomerular filtration rate (GFR) > 60 ml/min/1.73m² (stage 1 or 2 CKD, n=7), and non-diabetic control subjects (n=6). The risk of NSF was considered very low given the volunteers’ GFR and the observed incidence of NSF (4). Blood glucose was maintained at 4.0 - 6.0 mM in diabetic volunteers by intravenous insulin infusion. Microalbuminuria volunteers were receiving ACE inhibitor or angiotensin II receptor blocker medication, which alter renal haemodynamics. Experiments were performed whilst taking and 4 weeks after stopping drug treatment. Data were acquired on a 3T Philips Achieva scanner using a cardiac array receive coil. Volunteers attended fasting at 8am. Baseline MRI scans were acquired, consisting of phase-contrast angiography (FFE, TR/TE = 5.1/1.6 ms, tip = 10°, 6 mm slice, scan time = 20 sec, cardiac gated breath-hold) to measure renal artery flux over the cardiac cycle and multiple gradient echo imaging to produce R2* maps (TR = 106 ms, 61 echoes with TE 1-51ms, 13 sec breath-hold, 224x122 matrix over 360 x 270 mm FOV). Subjects then consumed 20 ml water per kg body weight. Urine output was monitored after water loading and MRI measurements repeated when urine flow was >8 ml/min. 3D Gd-enhanced images were acquired (3D-FFE, TR/TE=5.1/1.6 ms, tip = 30°, 17 sec acc) when urine output had decreased below 5 ml/min using Magnevist contrast agent at a dose of 0.2 ml/kg. Data was excluded if the kidney had more than one renal artery. Phase contrast quantitative flow measurements were analysed using ViewForum software (Philips Medical Systems). An ROI was drawn around the renal artery to determine flux at each acquired timepoint in the cardiac cycle, and total flux over the cycle calculated. Flux measurements were scaled by body surface area for comparison between subjects. R2* maps were generated from mGRE datasets using custom software written in Matlab. Cortical and medullary ROIs were chosen based on anatomic information from T1-weighted and Gd-enhanced images, and the change in cortical and medullary R2* following water loading determined from these ROIs. Cortical and medullary volumes were calculated using Osirix software (www.osirix-viewer.com) from 3D Gd-enhanced image datasets acquired immediately after (showing cortex) and 5 minutes after (showing cortex + medulla) Magnevist administration. Statistical analysis employed a 1-way ANOVA with Scheffe posthoc multiple comparisons.

Results and Discussion

Figure 1: Representative data showing the change in T1-weighted image signal intensity at 30 sec and 5 min after contrast agent administration, and ROIs generated from these data to calculate cortical and medullary volumes. Figure 2 shows cortical and medullary volumes in the three experimental groups. No statistically significant difference was observed between groups. Figure 3 shows renal artery flux measurements from controls, normal T1D and microalbuminuria T1D subjects without and with ACE inhibitor medication. For both pre- and post-water loading, lower flux was observed in the Type 1 diabetic groups compared to control subjects (p < 0.015). Microalbuminuria T1D subjects (no ACE inhibitors) had lower flux than normal T1D subjects (p = 0.03). No statistically significant differences in renal artery flux were observed between the T1D groups. Contrary to other studies (4), we found no changes in R2* that could be ascribed to changes in renal oxygenation in any of the experimental groups (Figure 4: representative R2* maps).

Conclusions

The two Type 1 diabetic groups exhibited lower renal artery flux than observed in the control group. T1D subjects with microalbuminuria appeared to show lower renal artery flux than normal T1D subjects, and this difference may be reduced by ACE inhibitor treatment, though further studies are required to confirm this finding. There was no difference in kidney volumetrics between control, normal T1D, and T1D with microalbuminuria groups. BOLD measurements showed no changes in kidney R2* that could be ascribed to changes in medullary oxygenation. Alternate MRI approaches for early detection of diabetic nephropathy could test perfusion measurements such as dynamic contrast-enhanced imaging or arterial spin labelling.

Acknowledgements and References