Renal Diffusion and Perfusion in Cardiorenal Syndrome.

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Background Despite its clinical importance, the pathophysiology of chronic cardiorenal syndrome (CRS) is currently not fully understood [1]. Renal dysfunction (RD) is one of the most important independent risk factors for poor outcomes and all-cause mortality in patients with congestive heart failure (HF). However, it is not understood whether this renal dysfunction is caused by changes in tissue structure (fibrosis) or haemodynamic changes.

Aim To assess MR diffusion and perfusion of the kidney in patients with cardiorenal syndrome compared to healthy volunteers (HV), to assess pathophysiology.

Methods 35 subjects were enrolled into four groups: Group 1: 10 HV <40yrs; Group 2: 10 HV >50yrs (BSA corrected ejection fraction, EF=36±2%); Group 3: 8 stable HF without RD (57-82yrs, eGFR>60mL/min, EF=16±2%); Group 4: 7 stable HF with RD (62-78yrs, eGFR<60mL/min, EF=25±3%). All imaging was performed using a 1.5T Philips Achieva scanner (body transmit coil, 16-channel SENSE torso receive coil) in a single session. Multi-slice True-FISP data was acquired in 3 orthogonal planes to locate organs/vessels. *Diffusion*: Respiratory triggered spin echo (SE) DWI data (288×324 mm FOV, 5 or 10 coronal-oblique slices (3×3x8 mm or 3×3x5 mm voxel) was collected with an EPI readout (TR/TE = 3.2 s/71 ms) at 10 b-values (b = 0, 50, 100, 150, 200, 250, 300, 500, 750, 800 s/mm^2) and 6 orthogonal diffusion directions. *Perfusion*: Respiratory-triggered ASL data (matched in geometry to DWI, label delay = 1100 ms, in-plane pre-saturation, 30 pairs) were collected with a True-FISP readout (TE/TR 2.1/4.1 ms, SENSE 2, FA 60°, centric half-Fourier acquisition) [2]. Base magnetization images and inversion recovery data were acquired to form M_0 and T_1 maps. *Vessel Flow*: PC data were collected for both renal arteries (RA) using a single slice TFE sequence perpendicular to each vessel (15 phases, TR/TE 6.9/3.7 ms, FA 25º, NEX 2, 1.17x1.17x6 mm^3, TFE factor 4-6 (dependent on subjects' heart rate), V_{ENC} = 100cm/s, single breath hold per vessel).

Data Analysis*: *Diffusion: DWI images were averaged across directions for each b-value. A renal cortex mask was created for each kidney/slice by thresholding the T_1 map. This was used to generate average DW cortex data for each b-value. The ROI data was then fit to a monoexponential diffusion model for ADC, and a biexponential model for D, D* and f_p, the product of D* and f_p was also calculated as a marker of total flow. Monte Carlo simulations (1000 repeats, SNR 50:1) were performed simulating the diffusion data (ADC: 2.4, D: 1.8, D*: 15x10^{-3} mm^2/s, f_p: 30 %) to assess the accuracy and standard deviation of the mean fitted value.

Perfusion: ASL images were motion corrected to the base M_0 image using FSL (FMRIB Software Library) and difference images (label-control) calculated and averaged to create a single difference map (ΔM). A perfusion map was formed using a kinetic model using the individuals' ΔM, base M_0 image and tissue T_1 [3]. The renal cortex mask was used to calculate the mean perfusion across both kidneys. *Vessel Flow*: Philips Q-flow software (Philips Medical Systems) was used to draw a region of interest (ROI) over the vessel, and the mean area, flow velocity (cm/s) and flux (ml/s) over the cardiac cycle, across the vessel, calculated.

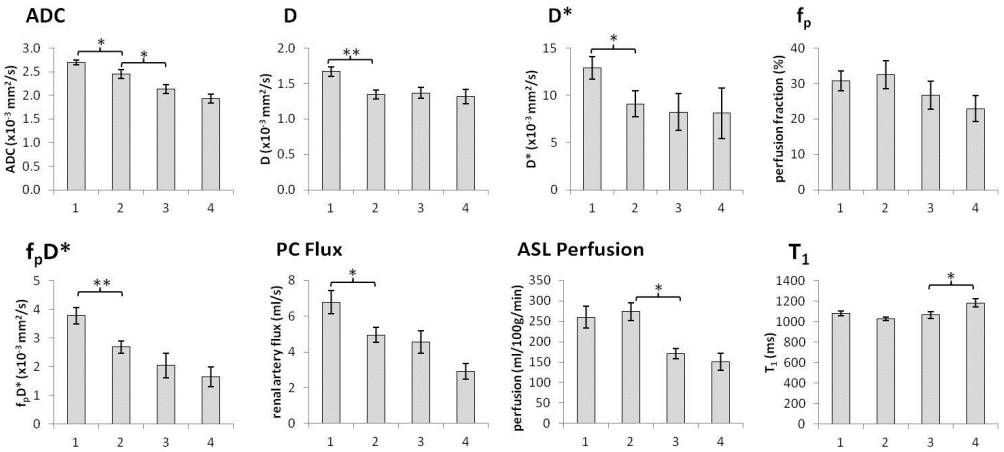

Figure 1: (Mean ± SEM) Renal cortex ADC, D, D*, fp, fD*, renal artery flux, renal cortex perfusion and T_1 for each group (1: HV <40yrs, 2: HV >50yrs, 3: HF w/o RD, 4: HF w/ RD). **p<0.01, *p<0.05.

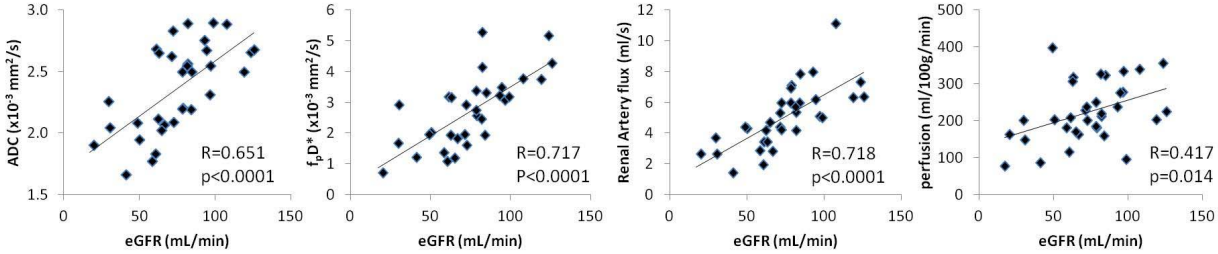

Figure 2: Renal cortex ADC, f_pD^* renal artery flux and renal cortex perfusion against eGFR, with Pearson correlation coefficient (R).

Statistics: (SPSS 18) Independent paired tests were made for ADC, D, D*, f_p, f_pD^*, flux and perfusion for groups 1v2 (HV <40yrs and >50yrs), groups 3v4 (HF with and without RD) and groups 2v3 (HV v HF w/o RD). Pearson correlation coefficients (R) were assessed.

Results

Figure 1 shows the cortex ADC, D, D*, f_p, f_pD^*, renal artery flux and renal cortex perfusion, with a reduction in ADC, f_pD^*, flux and perfusion across groups 1-4. Monte carlo simulations show an accuracy of (-0.1,1.5, 5.9,3.0, 2.3)% and stdev of (2.6,9, 31, 18, 12)% for ADC, D, D*, f_p and f_pD^* respectively. There is a significant difference in ADC, D, D*, f_pD^* and flux between the two HV groups, and between the HV >50yrs group and HF w/o RD group for ADC and perfusion. The only significant difference between HF patients with and without renal dysfunction is for T_1. Figure 2 shows significant correlations of ADC, f_pD^*, flux and perfusion with eGFR. D is also highly correlated with eGFR (R=0.483, p=0.005, not shown). f_pD^* is correlated with both renal artery flux and renal cortex perfusion (R=0.562, p=0.001 and R=0.407, p=0.021 respectively). T_1 correlated negatively with eGFR values (R=-0.436, p=0.01) and was prolonged in HF patients with renal dysfunction compared to those HF without renal dysfunction. There was no significant correlation of ADC or D with T_1.

Discussion and Conclusion

Results suggest that flow, as demonstrated by f_pD^*, contributes significantly to the changes in ADC, and that these changes are correlated to PC flux and ASL perfusion measures. However, although there was no difference between HF groups in f_pD^*, there is a trend for reduced fpD*, PC Flux and perfusion with severity of disease. In addition structural changes are reflected by the increase in T_1, though these are not reflected in D alone. Renal dysfunction in heart failure is mediated by decreased renal perfusion. Further, prolonged T_1 reflecting chronic structural renal changes/congestion might be the primary culprit in the pathophysiology of the chronic cardiorenal syndrome. These structural changes appear to be associated with classical cardiovascular risk factors.

References: [1] Ronco et al. Blood Purif 2009; **27**:114-126, [2] Gardener et al. MRM 2010; **63**:1627-36, [3] Buxton et al. MRM 1998; **40**:383-96