

Renal cortico-medullary differentiation in liver cirrhotic patients: Is the pathology cortical or medullary or both?

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Introduction: Liver cirrhosis patients are frequently affected by renal compromise with the progression of the disease (1, 2). In this patient population, and as reported for other pathologies previously (3-5), visual decrease in corticomedullary differentiation (CMD) is observed with increasing renal insufficiency by T1-weighted MRI. We explored differences in T1 values for renal medulla and cortex and their role in producing decreased visual differentiation within the failing kidney.

Materials and Methods: 33 (M/F: 22/11) liver cirrhosis patients, aged (40 - 70 yrs), referred for HCC screening were recruited to additionally undergo same day ^{99m}Tc-DTPA renography to determine single kidney glomerular filtration rate (SKGFR). Patients with an estimated GFR (eGFR) <15 ml/min/1.73m² were excluded from the study. All patients provided written informed consent. MRI was performed at 1.5T (Avanto; Siemens Medical Solutions, Erlangen, Germany) and included T1 measurements using a free breathing spoiled gradient echo saturation recovery turboFLASH images with a single coronal slice through the long axis of both kidneys and an axial slice through the middle of each kidney with the following parameters: TR/TE/FA = 526 ms/1.21 ms/16°, FOV= 420mm x 382mm, GRAPPA acceleration factor 2, “inversion” time 300 ms. T1 values in the renal cortex and medulla were determined from signal intensity values using the longitudinal relaxation equation $[SI(t) = M_0 \times (1 - e^{-T1/T1})]$ where M_0 was determined by repeating the sequence without the saturation prepulse and with TR = 4000 ms to obtain proton-density weighted images. Corticomedullary differentiation (CMD) was calculated as the difference in measured T1 values from the cortex and medulla. Pre-contrast 3D T1-weighted gradient echo imaging of the liver, performed as part of the clinical scan (TR/TE/FA = 3.79 ms/1.36 ms/12°) was extended to include the kidneys. Single kidney function was measured by renal clearance of ^{99m}Tc-DTPA (5 - 5.5 mCi IV injection), and calibration for split renal function was determined by external detection using standard coronal gamma imaging. GFR was measured by urinary clearance of the radioisotope requiring venous blood samples and urine collections over a 4 hour period. GFR was determined as an average of two sample periods each lasting 90 min each. Statistical analysis was performed using GraphPad Prism5.01.

Results: SKGFR values ranged from 5.4 to 63.8 ml/min/1.73m². T1 values ranged from 390 to 1148 msec in the cortex and 506 to 1782 msec in the medulla. By linear regression analysis (Fig. 1) CMD was significantly correlated with SKGFR (slope = 7.05 ± 1.56; 95% CI = 3.9 - 10.2; r = 0.5; p = <0.0001, Fig. 1). Medullary T1 values also showed a significant positive correlation with kidney function (slope = 9.3 ± 2.4; 95% CI = 4.5 - 14; r = 0.43; p = 0.0003). Cortex T1 values showed only a slight trend to shortened T1 with increasing insufficiency (r = 0.18; p = 0.15). On the basis of National Kidney Foundation guidelines for chronic kidney disease (6), stage 1 subjects (n=11) had an average CMD of 462.1 ms ± 129 ms, stage 2 (n =39) averaged 385 ms ± 131 ms, and stage 3 (n =16) averaged 338 ms ± 215 ms. Stage 4 and 5 could not be reliably assessed due to a limited number of subjects.

Discussion: CMD loss has been studied in a variety of pathologic states including but not limited to acute allograft rejection, glomerulonephritis and obstructive hydronephrosis (3-5) but the underlying mechanisms have not been identified. In hypertensive patients, Lee et al (7) showed decreasing CMD could be attributed to increases in cortical T1 values and relatively stable medullary T1 values with increased renal insufficiency. Leung et al (8) explained that preservation of CMD in ATN was associated with increased medullary T1 values with unchanged cortical values. With a significant decrease in medullary values and a slight decreasing trend in cortical T1 values with renal insufficiency in cirrhotics, our results suggest different pathologic mechanisms may lead to decreased corticomedullary differentiation in different disease states. T1 values may provide a valuable tool to begin to investigate underlying disease processes.

References: 1. Gines et al. NEJM 2009; 361:1279-1290; 2. Mackelaite et al. MCNA 2009; 93:855-869, viii; 3. Leung et al. AJR 1984;143: 1215-1227; 4. McCreath et al. BJR 1988;61:113-117; 5. Marotti et al. MRM 1987;5:160-172; 6. National Kidney Foundation. AJKD 2002;39(2 Suppl 1):S1-266; 7. Lee et al. JMRI 2007 Apr;25(4):790-5. 8. Leung et al. AJR 1984;143: 1215-1227

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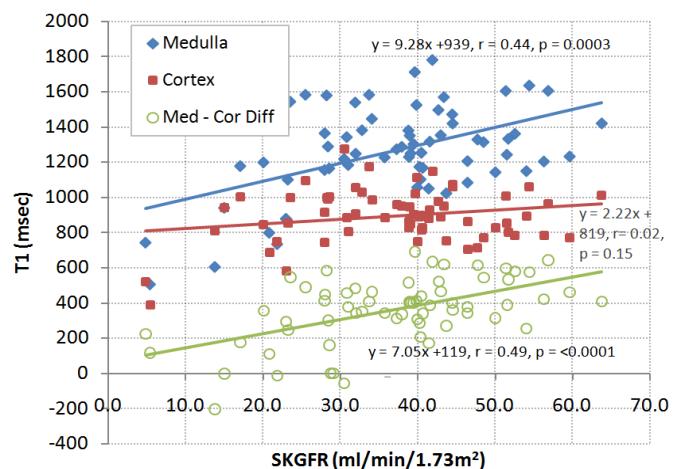


Figure 1. Linear regression analysis of T1 relaxation times of medulla and cortex and medullary cortical difference (CMD) plotted against single kidney glomerular filtration rate (SKGFR).

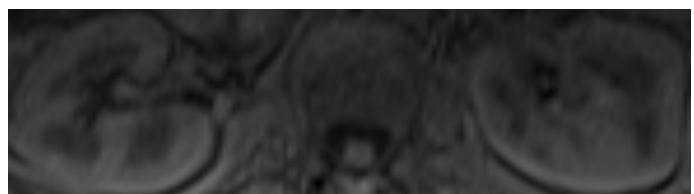


Figure 2. Axial T1-weighted image from patient with left kidney SKGFR of 39.1 ml/min/1.73m², cortical T1 = 849 msec and medullary T1 = 1251 msec. Right kidney SKGFR measured 38.9 ml/min/1.73m², cortical T1 = 829 msec and medullary T1 = 1231 msec.

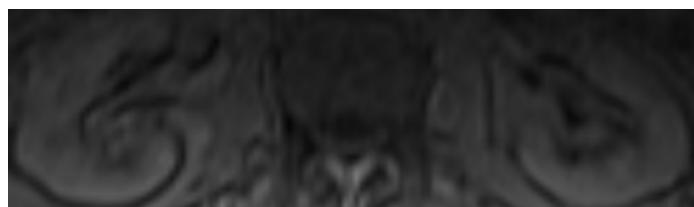


Figure 3. Axial T1-weighted image from patient with left kidney SKGFR of 17.1 ml/min/1.73m², cortical T1 = 1001 msec and medullary T1 = 1179 msec. Right kidney SKGFR measured 15 ml/min/1.73m², cortical T1 = 943 msec and medullary T1 = 941 msec.