Functional MRI Demonstrates Dynamic Alteration in Renal Glomerular Filtration Rate Following Angiotensin Converting Enzyme Inhibition

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INTRODUCTION

An activated renin-angiotensin system is seen in hemodynamically significant RAS, and demonstration of response to ACE inhibitors has been used as an indicator of patient prognosis in renovascular hypertension [1]. MRI has the unique ability to non-invasively measure kidney function and depict blood vessel anatomy, therefore potentially combining the structural and functional assessment of renal artery stenosis (RAS). Dumoulin and Katzberg *et al*. first introduced a noninvasive MR method for measuring single kidney GFR after an injection of Gd-DTPA [2] and the method has been used to diagnose RAS [3]. However, the dynamic alterations in renal physiology following ACE inhibition have not been demonstrated to date, except by invasive means. The objective of this study is to investigate the acute physiologic effect of ACE inhibition on renal filtration in swine with renal artery stenosis.

MATERIALS AND METHODS

Five medium sized (50-65 lb) swine with surgically implanted MRI-compatible ameroid constrictors (Research Instruments SW, Escondido, CA) around the main renal artery were imaged under a protocol approved by the University of Wisconsin Research Animal Resources Center. Magnetic resonance imaging was performed on a 1.5 T MR scanner (GE Medical Systems, Milwaukee, WI) using a torso phased array or cardiac coil. Heart rate, respiration and blood pressure were monitored. A 3D-MRA was performed to obtain anatomical information (Figure 1). Renal blood flow (RBF) was determined using 2D phase contrast MRI. Extraction fraction was measured using a previously validated inversion-recovery Look Locker (LL) method with EPI and SSFP readout [4,5]. Phase contrast scans used a matrix of 256 x 192, FOV of 24 cm and the VENC ranged from 40-100 cm/s. EPI LL (TR/TE/Flip = 2500 ms/12.5ms/ 90°) and SSFP sequences (TR/TE/Flip = 4.5 ms/1.9ms/50°) were used to determine the extraction fraction. The FOV was either 24 or 30 cm, the slice thickness was 5.0 mm, and a matrix of 128 x 128 for EPI LL and 256x 256 for SSFP. Baseline measurements were obtained. Enalaprilat, an ACE inhibitor, was intravenously administered. Scans were repeated at 0, 15, 30, and 45 minutes post Enaloprilat. Post processing was completed offline to calculate RBF, EF and skGFR. Average skGFR values were obtained for the four swine with stenosis greater than 60%.

RESULTS AND DISCUSSION

Data from the stenotic kidney was averaged for RAS greater than 60%. The RBF and EF in the case of an 80% stenosis are shown in Figure 2. The RBF remained relatively constant over the 45 minutes time period. Average RBF was 95.1, 81.7, 84.2 and 99.3 ml/min at 0, 15, 30 and 45 minutes respectively. Preliminary *in vivo* measurements of the EPI LL and SSFP suggest the SSFP to be a better method for calculation of the extraction fraction due to less susceptibility artifacts leading to better image quality. The EF value exhibited a change post Enalaprilat, dropping near zero filtration at 15 minutes. It then slowly increased close to the initial EF value. Combining EF and RBF measurements, skGFR is determined. Average values were calculated and plotted over time (Figure 2). At 15 minutes post Enalaprilat, a sharp decrease in skGFR was observed, with recovery at 45 minutes. While this finding is expected, and has been observed with invasive studies, the MRI method provides a rapid non-invasive assessment of renal dynamics.

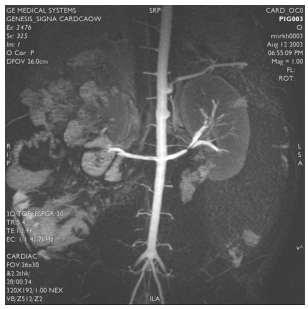

Figure 1: (Left) 3D MRA. RAS was confirmed in the left kidney through 3D-MRA.

CONCLUSIONS

An ACE inhibitor's effect on renal filtration can be monitored dynamically with MRI. An acute change in skGFR due to an ACE inhibitor was observed with MR imaging at fifteen minutes in animals with hemodynamically significant RAS.

We gratefully acknowledge funding from NIH Grant HL67029.

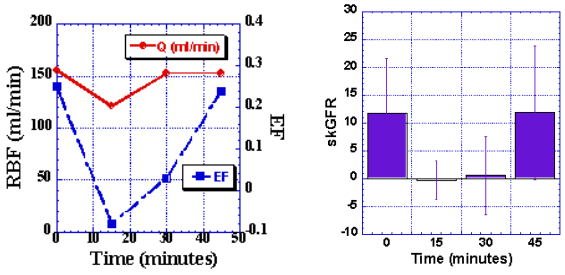

Figure 2: (Left) Extraction Fraction and Renal Flow Rate over Time. A drop in EF (blue) was seen 15 minutes post Enalaprilat while RBF (red) remained relatively constant.

(**Right) Average skGFR for RAS Greater than 60%.** A decrease in skGFR occurred at 15 and 30 minutes post Enalaprilat.

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