

Oxygen Bioavailability and Pulse Wave Velocity in Patients with Metabolic Syndrome

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INTRODUCTION

Metabolic syndrome (MS) is a defined cluster of medical disorders that includes obesity, hypertension, insulin resistance, and lipid abnormalities. The presence of MS increases future risk of Type II diabetes mellitus and atherosclerotic cardiovascular disease (CVD). MS is associated with arterial stiffening and increased aortic pulse pressure. It has been postulated that increased aortic pulsatility may lead to renal barotrauma and altered renal function. MRI techniques have been developed that allow for the evaluation of CV and renal health noninvasively. Pulse wave velocity (PWV) with a series of 2D phase contrast (PC) scans has been used to assess aortic stiffness [1-2]. Blood oxygen-level dependent (BOLD) MR techniques allow for the regional assessment of oxygen bioavailability in the kidney [3-4]. The purpose of this study was to assess aortic stiffness and renal oxygen bioavailability in patients with metabolic syndrome using MR-based PWV and BOLD techniques. We hypothesized that metabolic syndrome would be associated with significantly increased PWV and with changes of oxygen bioavailability indicative of renal dysfunction.

MATERIALS & METHODS

This HIPAA-compliant study was approved by our institutional human subjects review committee and written informed consent was obtained from all subjects. Five patients with metabolic syndrome (2 men, 3 women; ages 50-67; age: 59.2 ± 7.2 years; BMI: 39.2 ± 5.8 ; eGFR (MDRD) = 86.2 ± 18.6 ml/min/1.73m²) were imaged with a 1.5T MR scanner (Signa Excite HD, GE Healthcare, Waukesha, WI, USA) and an 8-channel body coil. All five patients were non-diabetic with slightly elevated HbA1c (mean = $6.3 \pm 0.8\%$) and normal non-fasting glucose levels (mean = 107 ± 13.6 mg/dl). Subjects fasted for four hours prior to the MR examination.

A product 2D PC sequence with prospective ECG gating and optimized temporal resolution (~22-32ms temporal resolution) was used for flow imaging in the ascending aorta, aortic arch, and in the proximal, supra-diaphragmatic, and infrarenal descending aorta. Slices were prescribed as double oblique to the vessel lumen as determined from a contrast-enhanced MR angiogram using a single dose (0.1 mmol/kg) of gadobenate dimeglumine. Scan parameters included a TR/TE/flip angle = 6.1ms/3.7ms/30°, FOV = 32-34cm, VENC = 150cm/s with through-plane flow encoding, a slice thickness of 8mm, 488 Hz/pixel, and a 256x256 encoding matrix with a 70% phase FOV. Each 2D slice was acquired in a breath hold. PWV was derived from the series of 2D PC scans using a custom-built MATLAB tool (v7.9, The MathWorks, Cambridge, MA) as previously described [5]. PWV was measured with both the time-to-foot (TTF) and cross-correlation (XCorr) techniques.

For PWV results, four age-matched healthy subjects (2 men, 2 women; ages 48-59 years; mean: 53.5 ± 4.7 years; BMI: 25.9 ± 5.0) from a previous study [5] were used for comparison to the patients with MS. Differences in PWV between healthy subjects and MS patients were compared with a Welch's t-test.

MR BOLD images were acquired with a TR/TE/flip angle = 87ms/7-42ms/40°, FOV = 32-34cm, 244 Hz/pixel, and a 256x128 matrix. Each of five slices was acquired in a separate 12-second breath hold. R_2^* (s⁻¹) measurements of medullary and cortical oxygen bioavailability were measured from BOLD images as previously reported [6]. Measurements in the medulla and cortex were averaged across all five slices for each subject.

For BOLD results, five age-matched controls (ages 52-62 years; mean: 55.2 ± 4.3 years; eGFR (MDRD): 74.6 ± 6.2 ml/min/1.73 m²) from a previous study were used for comparison to the patients with MS. Differences in oxygen bioavailability between healthy subjects and MS patients were compared with a Welch's t-test.

RESULTS

For PWV results, no significant difference was found in the ages of the two groups ($p=0.20$). PWV values were significantly greater in patients with MS for both the TTF ($p=0.02$) and XCorr ($p=0.01$) techniques (8.4 ± 2.0 and 10.1 ± 2.1 m/s for the TTF and XCorr techniques, respectively) than in healthy volunteers (5.4 ± 0.6 and 5.4 ± 0.9 m/s for the TTF and XCorr techniques, respectively; Figure 1).

For BOLD results, no significant difference was found in the ages of the two groups ($p=0.59$). Medullary R_2^* values were significantly lower in MS patients (17.8 ± 1.6 s⁻¹) than in healthy volunteers (20.6 ± 1.1 s⁻¹; $p<0.001$). No significant difference was found in cortical R_2^* values between MS patients (11.1 ± 0.7 s⁻¹) and healthy volunteers (11.7 ± 0.9 s⁻¹; $p=0.10$). R_2^* maps from both healthy participants and MS patients depict color differences in medullary values (Figure 2).

DISCUSSION & CONCLUSIONS

The elevated PWV values found in MS participants are consistent with increased aortic stiffness. Elevated PWV is typically associated with increased pulsatility in the central circulation, which may transmit into the kidney due to the short intervening arteriolar distance. Furthermore, the association of increased PWV and altered renal tissue oxygenation, as well as the known increase in renal dysfunction with advanced MS, suggests that arterial stiffening may play a causal role in renal dysfunction and future risk. Other investigators have noted increased renal vascular resistance potentially related to increased arterial wall stiffness in a group of diabetic patients [7]. Note that the 2D PC slices were acquired in sufficiently low scan time for a breath hold, despite the disease state of the subjects, and still provided sufficient temporal resolution to resolve the elevated PWV.

BOLD results demonstrated significantly lower medullary R_2^* values in patients with metabolic syndrome, which indicates that these patients have relatively elevated medullary oxygen bioavailability in comparison to healthy volunteers. Previous studies have shown that medullary oxygen bioavailability is elevated in patients with renal allograft dysfunction and in patients with diabetes [6,8]. However, in both of these studies the eGFR was decreased in the groups with decreased R_2^* . Therefore it is interesting that in our metabolic syndrome group where the R_2^* is decreased, the eGFR is not decreased relative to the age-matched healthy subjects. Future larger studies may help elucidate the use of BOLD and PWV in the early changes in renal function, which may occur before there are changes in patients' renal function as measured by eGFR.

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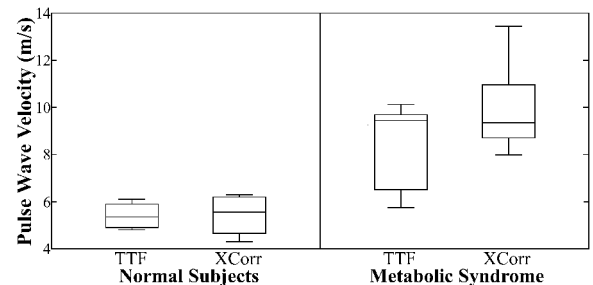


Figure 1. Box plots of pulse wave velocity as computed with the time-to-foot (TTF) and cross-correlation (XCorr) techniques for five patients with metabolic syndrome and four age-matched normal controls.

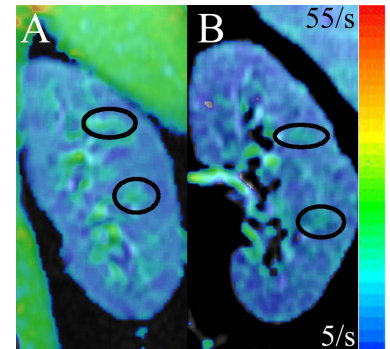


Figure 2. R_2^* maps from MR BOLD images in a healthy volunteer (A) and a patient with MS (B). Medullary pyramids are circled. Medullary R_2^* values are greater (more green) in healthy subjects than in MS patients.