Aortic Pulse Wave Velocity Measured using4D-Flow MRI in Patients with Portal Hypertension

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TARGET AUDIENCE Clinicians and scientists interested in liver, cardiovascular, and metabolic disease.

PURPOSE Diffuse liver disease, such as non-alcoholic fatty liver disease (NAFLD), causes a generalized pro-inflammatory response that has systemic effects. As a result, patients have an increased risk for developing coronary plaques and atherosclerosis leading to cardiovascular disease[1-7]. MRI can provide the means to non-invasively identify and risk-stratify both liver and cardiovascular disease. Aortic pulse wave velocity (PWV) is a biomarker of vascular stiffening[8,9] and can therefore indicate increased cardiovascular risk. We therefore hypothesized that aortic PWV would be elevated in the setting of cirrhosis and portal hypertension. The ***purpose of this study*** was to measure aortic PWV in subjects with portal hypertension and in healthy controls.

METHODS In this prospective, institutional review board approved, and HIPAA-compliant study, 11 patients with portal hypertension due to alcohol abuse (n=5), hepatitis C (n=4), and other causes (n=2) were recruited. Diagnosis of portal hypertension was determined either by clinical history or from imaging features of portal hypertension (eg. definite varices, splenomegaly) from recent clinical MRI studies. In addition, 13 healthy subjects with no known liver disease were recruited as controls. Written informed consent was obtained from all subjects prior to inclusion. 4D flow MRI was conducted on a clinical 3T scanner (Discovery MR750, GE Healthcare, Waukesha, WI) usinga 32-channel phased-array body coil (NeoCoil, Pewaukee, WI). 4D flow MRI was performed with a five-point, radially undersampled phase contrast acquisition (PC VIPR) due to its increased velocity sensitivity performance complete coverage of the upper abdomen, and isotropic spatial resolution[10-12]. Image parameters included: imaging volume: 32x32x24 cm^3 spherical centered over the celiac axis, 1.25 mm acquired isotropic spatial resolution. Data were reconstructed to 14 time frames per cardiac cycle. The time-averaged 3D PC MR angiograms were used to automatically position 20 virtual 2D planes along the entire descending aorta using a manually placed spline (Figure 1a). Cut plane placement, flow quantification, and visualization were all performed in EnSight visualization software (v. 10.0, CEI, Apex, NC). Exported flow waveforms (Figure 1b) were loaded into Matlab (Mathworks, Natick, MA), upsampled to 400 time points, and analyzed using several methods including time-to-peak (TTP), time-to-upstroke (TTU), time-to-foot (TTF), and cross-correlation (XCOR). The time shifts were plotted against the distance between the planes. PWV was calculated as the inverse slope of the linear line fitted to the data (Figure 1c). Aortic PWV values were compared between patients with portal hypertension and healthy volunteers.

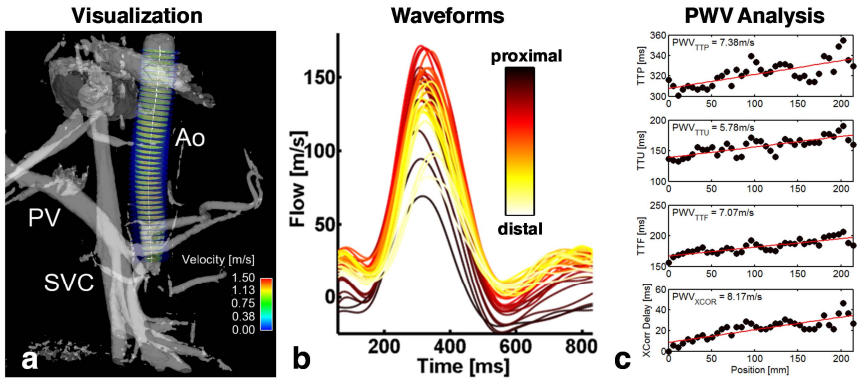

Figure 1*. Pulse wave velocity(PWV) analysis for the descending aorta. a) A spline is manually placed down the centerline of the descending aorta (Ao). Analysis planes are automatically placed along the spline. b) Flow waveforms are recorded from each analysis plane. c) The time shifts are plotted against the distance between planes. PWV is calculated by taking the inverse slope of the line fitted to the data.*

RESULTS Aortic PWV, as calculated using the TTF method, demonstrated statistically significant (p=0.01) differences between the two groups(Figure 2). The TTF method also showed the least variability between subjects. The other 3 methods did not show statistically significant differences (p>0.05).

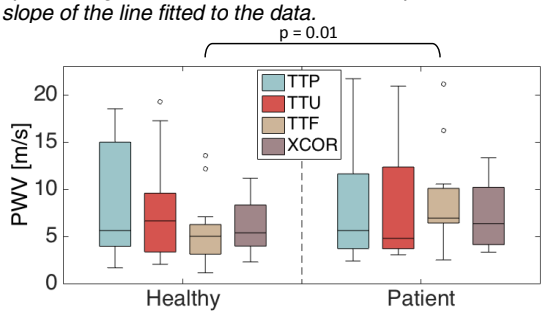

Figure 2. *Aortic PWV of patients with portal hypertension compared to healthy volunteers. The time-to-foot (TTF) method resulted in statistically significant differences between the two groups (p=0.01).*

DISCUSSION AND CONCLUSION We have used 4D flow MRI to measure increased aortic PWV in patients with portal hypertension using the TTF method. This is the method that has shown to be most robust in prior work as well[13]. This technique is non-invasive and provides vessel velocimetry over a wide volumetric coverage with high spatial resolution. Normal aging leads to aortic inflammatory changes that also results in aortic remodeling and has a role in cardiovascular disease. A larger study with age-matched controls could enable distinction between age-related increases in aortic PWV versus those that are disease-related. In addition, further classifying the results according to causes of cirrhosis (ie. Hepatitis C[1]vs. NAFLD) may be critical to understanding how these disease processes impact cardiovascular disease.

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