Non-Invasive Characterization and Staging of Portal Hypertension using 4D Flow MRI

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Target audience: Clinicians and researchers interested in cirrhosis and portal hypertension.

Introduction: Portal hypertension (PTHN) is an end-stage complication of cirrhosis that leads to complex anatomical (portosytemic collaterals) and hemodynamic alterations in the hepatic circulation. The Child-Pugh score employs a combination of clinical parameters to assess the prognosis of cirrhosis, however it does not directly include alterations in blood flow [1]. Azygos flow has been previously reported as being directly related to portal pressure [1]. Currently, there are few valid quantitative biomarkers to assess blood flow to and from the liver. Phase contrast 4D-flow MRI methods have shown to be feasible for assessing hemodynamics in the abdomen [2,3,4]. ***The purpose of this study*** was to evaluate 4D flow MRI as non-invasive method for characterizing and staging patients with portal hypertension.

Methods: In this IRB-approved and HIPAA-compliant study, 19 patients (53±13years, 76±24kg) with portal hypertension, evidenced by the presence of varices and splenomegaly, were imaged after written informed consent was obtained. Patients were scanned after at least 5 hours of fasting (baseline). A second scan was performed 20 minutes after a meal challenge [5].

MR-Imaging. Studies were conducted on a clinical 3T scanner (Discovery MR 750, GE Healthcare, Waukesha, WI) with a 32-chanel body coil (NeoCoil, Pewaukee, WI). 4D velocity mapping was achieved using a radially undersampled phase contrast acquisition (5-point PC-VIPR) with increased velocity sensitivity performance [6,7]. Radial 4D flow MRI image parameters included: imaging volume: 32x32x24cm spherical, 1.25mm acquired isotropic spatial resolution, TR/TE=6.4/2.2ms. All subjects received 0.03mmol/kg of gadofosveset trisodium (Lantheus, N. Billerica, MA), an intravascular gadolinium based contrast agent used to maximize SNR performance and injected prior to the pre-meal scan. Baseline and post meal challenge PC-VIPR imaging was adjusted for optimal imaging conditions and differed in the venc: (pre=100cm/s, post=120cm/s) and flip angle (pre=16°, post=14°).

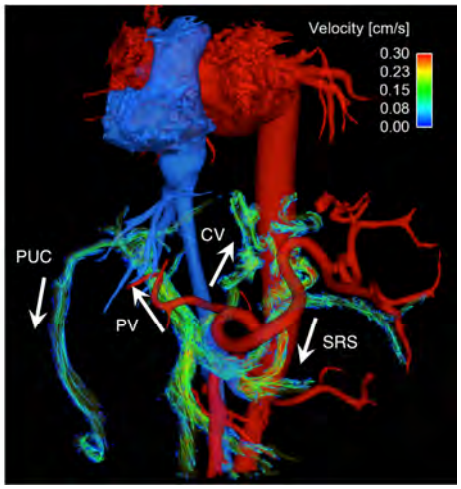

Figure 1– Visualization post meal in a 51 yo male with portal hypertension. Hepatofugal flow (white arrows) through the paraumbilical collateral (PUC), coronary vein (CV) and splenorenal shunt (SRS).

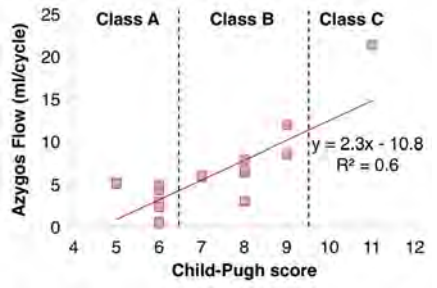

Figure 2– Linear correlation between baseline Azygos flow and the Child-Pugh score. Dashed lines depict the intervals for the Child-Pugh classification of cirrhosis stage.

4D flow MRI Data Analysis: *V*essel segmentation was performed in MIMICs (Materialize, Leuven, Belgium) from PC angiograms and manual placement of cut-planes in the vessel of interest in EnSight (CEI, Apex, NC) were flow measurements and visualizations were conducted. Flow data were acquired at the Superior Mesenteric Vein (SMV), Splenic Vein (SV), Portal Vein (PV), Azygos vein (Azy), and Collaterals (Col) (Fig1). Shunt fraction (% of total portal blood flow bypassing the liver through collaterals) was calculated as: $Q_{Col}/(Q_{SMV} + Q_{SMV})$

Statistics:). Flow values measured in each vessel were compared before and after the meal challenge using paired Student t-tests. A p-value of 0.05 was chosen to indicate statistical significance. In all patients the Child-Pugh score [1], a clinical staging of cirrhosis, was calculated. In addition, the Model for End-Stage Liver Disease (MELD) score was also calculated based on a recent serum creatinine, bilirubin and INR level [8]. Linear correlations were evaluated between flow measurements and clinical scores.

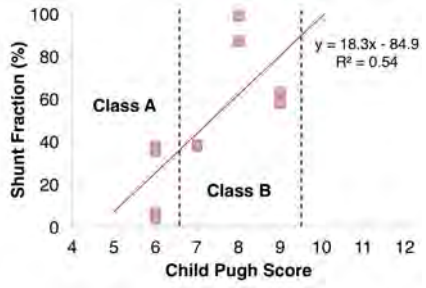

Figure 3– Linear correlation between baseline shunt fraction and the Child-Pugh score. Dashed lines depict the intervals for the Child-Pugh classification of cirrhosis stage.

Results and Discussion: Azy, SMV, SV and PV flows were successfully quantified in all patients (19/19) whereas collateral vessels were present (visible) in only nine (9/19) patients. Statistically significant increase in blood flow was seen in the PV (12.2 ± 7.3 vs 15.4 ± 9.4 ml/cycle; p=0.003) in response to the meal challenge. Similarly Azygos vein flow increased (5.9 ± 4.6 vs 6.5 ± 3.4 ml/cycle; p=0.4), however this increase was not statistically significant. A non-statistically significant increase was seen in the shunt fraction (48 ± 32 vs 57 ± 44 %; p=0.9) in response to the meal challenge.

However, good correlation was observed between baseline azygos flow and the Child-Pugh score ($r^2 = 0.6$) (Fig2). A significant difference was also found between azygos flow in class A and class B patients at baseline (3.5 ± 1.8 vs 6.6 ± 2.7 ml/cycle; p=0.047). Good correlation was also seen between shunt fraction at baseline and Child-Pugh score ($r^2 = 0.54$) (Fig3). No correlation was found between the MELD score and any of the hemodynamic parameters measured.

Summary: The ability to non-invasively quantify hemodynamic changes not only in normal vessels but also in collateral circulation demonstrates that 4D flow MRI may be a suitable tool for staging and monitoring treatment of patients with portal hypertension. Not surprisingly, we encountered highly patient-specific responses to the meal challenge. However based on these encouraging results we are currently enrolling additional patients to investigate the use of 4D flow MRI for improved characterization of the liver hemodynamics in patients with portal hypertension.

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References: [1] Bosh J Hepatol 1985 [2] Stankovic JMRI 2010; [3] Frydrychowicz JMRI 2011; [4] Roldán-Alzate JMRI 2012; [5] Roldán-Alzate ISMRM 2013; [6] Gu AJNR 2007; [7] Johnson MRM 2010; [8] Malinchoc Hepatol 2000.