4D Flow Analysis of Patients with Advanced Liver Cirrhosis: Correlation between Clinical Parameters And Flow Parameters

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Introduction: Patients with advanced liver cirrhosis present with a hyperdynamic syndrome with increased cardiac output, elevated splanchnic inflow and increased hepatic vascular resistance resulting in portal hypertension and decreased portal flow velocities [1]. 4D flow MRI is a non-contrast volumetric imaging technique that acquires a time-resolved tri-directional velocity dataset with full 3D coverage of liver and portal venous hemodynamics [2]. Recent studies illustrate the feasibility of non-contrast 4D flow MRI for the advanced visualization and quantification of the hepatic blood flow patterns of patients with advanced cirrhosis [3-5]. Furthermore they show the benefit of this user-independent technique compared to the clinical standard of Doppler Ultrasound for the evaluation of the hepatic vascular system. The aim of this study was to compare the flow parameters obtained from 4D flow MRI to the clinical parameters of patients with liver cirrhosis represented by the Child-Pugh and MELD scores.

Methods: 4D flow MRI of the hepatic arterial and portal venous vasculature was applied in a cohort of 9 patients with liver cirrhosis (age= 58±5years). Each patient underwent a 4D flow MRI on a 3.0T MR system (Skyra, Siemens Medical Solutions, Germany). An axial oblique 3D volume was acquired with ECG gating and respiratory gating, using a navigator at the spleen-lung interface. Pulse sequence parameters were: spatial res.=2.5x2.1x3.0mm3, flip angle=15°, temporal res.=40.8ms, TE=2.7ms, averaged scan time 8.7min. A blood pool contrast agent was applied (Ablavar©, Lanteus, N. Billerica, MA). For the portal venous system a velocity encoding of 50cm/s was used; for the arterial system a venc of 100 cm/s was applied. Pre-processing was performed including noise filtering, anti-aliasing and eddy current correction. Flow evaluation of the hepatic arterial and portal system was performed by 3D visualization (EnSight, CEI, Apex, USA) including time-resolved particle traces originating from 10 emitter planes placed at anatomical landmarks of the liver vasculature (fig. 1). For quantitative analysis flow quantification was performed based on retrospective extraction of peak velocities and net flow over the cardiac cycle. Clinical blood parameters for the patients with advanced liver cirrhosis were evaluated based on the Child-Pugh score and MELD score including total bilirubin, serum albumin, serum creatinine, INR, presence of ascites and hepatic encephalopathy. Finally, correlation analyses were performed between the clinical parameters and the flow parameters calculated from 4D flow MRI.

Results: In this on-going study most of the patients presented with an early stage of liver cirrhosis. 7 out of 9 patients had Child-Pugh class A and 2 out of 9 Child-Pugh class B. Only 3 of the patients showed ascites as a complication of the disease and none of them presented with hepatic encephalopathy. The Child-Pugh score, based on 5 clinical parameters, offered a high correlation with the peak velocity in the extrahepatic splenic vein and the superior mesenteric vein, but also in the intrahepatic portal vein and the right portal vein branch as well as in the celiac trunk and splenic artery (r=0.737-0.916). The MELD score based on total bilirubin, INR and serum creatinine showed similar results for the splenic vein, intrahepatic portal vein and right portal vein branch as well as celiac trunk and splenic artery (r=0.608-0.740). The net flow values from the 4D flow MRI showed lower correlation to the Child-Pugh score parameters in the same vessels (r=0.441-0.862). The correlation with the MELD score was even lower for the net flow values in the splenic vein, intrahepatic portal vein, right portal vein branch as well as celiac trunk and splenic artery (r=0.358-0.673).

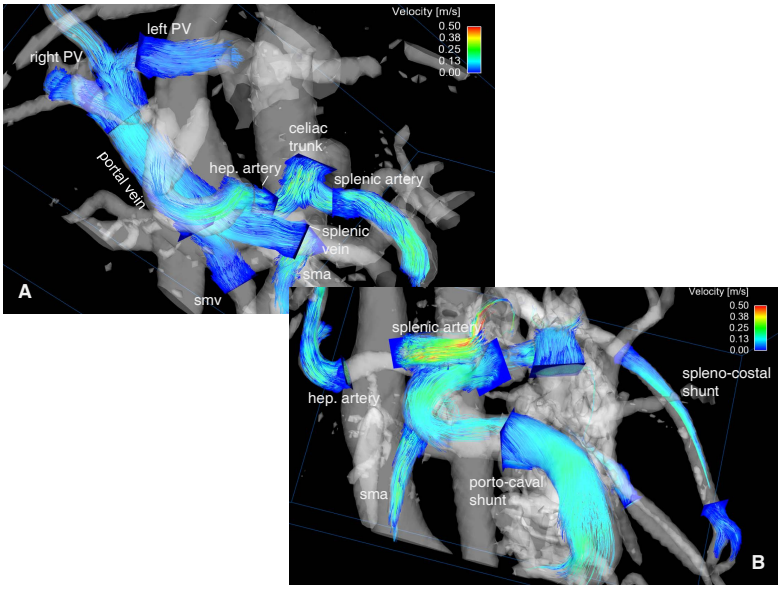

Figure 1: particle traces from emitter planes in the sup. mes. and splenic vein, prox. and distal spl.-mes.-confluence, right and left intrahepatic portal vein branch, celiac trunk, splenic, mesenteric and hepatic arteries. **A** normal physiological blood flow **B** patient with advanced liver cirrhosis presenting a large porto-caval shunt and multiple spleno-costal shunts in the back

pat. #	total bilirubin [µmol/l]	albumin [g/l]	INR	ascites	hepatic Encephalop.	creatinine [mg/dl]	Child-Pugh score	Child-Pugh class	MELD score
1	0.3	4.4	1.1	0	0	0.92	**5**	A	**2**
2	0.5	4.1	1.1	0	0	1.16	**5**	A	**6**
3	1.4	4.4	1.2	1	0	0.74	**6**	A	**7**
4	0.4	4.7	1	0	0	0.75	**5**	A	**0**
5	0.9	4.8	1.1	0	0	0.99	**5**	A	**7**
6	0.8	4.3	1.2	0	0	0.8	**5**	A	**5**
7	0.6	3.9	1	0	0	0.7	**5**	A	**1**
8	3.1	4.3	1.4	1	0	0.96	**8**	B	**14**
9	1.3	3.3	1.4	1	0	0.89	**7**	B	**10**

Table 1: clinical parameters of the patients with liver cirrhosis based on Child-Pugh and MELD scores

	peak velocity [m/s]									
	splenic vein	smv	spl.-mesent. confluence	intrahep. PV	right PV	left PV	celiac trunk	splic artery	hepatic artery	sma
bilirubin [µmol/l]	0.811	0.599	0.363	0.590	0.921	-0.154	0.817	0.894	-0.370	-0.011
albumin [g/l]	-0.034	-0.654	0.048	-0.609	-0.051	-0.300	-0.349	-0.245	-0.299	-0.241
INR	0.553	0.621	0.231	0.724	0.627	0.365	0.801	0.719	-0.044	0.209
creatinine [mg/dl]	0.210	0.161	0.284	0.504	0.215	0.727	0.406	0.464	-0.718	-0.548
Child-Pugh score	**0.737**	**0.782**	0.440	**0.773**	**0.842**	0.309	**0.916**	**0.916**	-0.150	0.184
MELD score	**0.608**	0.488	0.203	**0.740**	**0.731**	0.346	**0.729**	**0.740**	-0.383	-0.061
	net flow [ml/cycle]									
	splenic vein	smv	spl.-mesent. confluence	intrahep. PV	right PV	left PV	celiac trunk	splic artery	hepatic artery	sma
bilirubin [µmol/l]	0.644	-0.294	0.378	0.563	0.426	-0.062	0.643	0.884	-0.270	-0.210
albumin [g/l]	-0.034	-0.474	-0.096	-0.402	-0.445	-0.484	-0.042	-0.128	-0.105	0.078
INR	0.333	0.120	0.179	0.447	0.266	0.275	0.388	0.628	-0.170	-0.134
creatinine [mg/dl]	0.265	-0.404	0.048	0.104	-0.002	0.389	0.069	0.409	-0.794	-0.710
Child-Pugh score	0.543	-0.106	0.441	**0.658**	0.456	0.403	**0.621**	**0.862**	-0.287	-0.119
MELD score	0.459	-0.174	0.173	0.456	0.358	0.232	0.346	**0.673**	-0.386	-0.355

Table 2: correlation analyses for peak velocity and net flow over cardiac cycle and the clinical parameters for liver cirrhosis patients

Discussion: Our study subjects with mild stages of liver cirrhosis demonstrated a higher correlation between the peak velocities obtained by 4D flow MRI and the clinical scores based on blood parameters especially in the splenic vessels, the greater intrahepatic vessels and the celiac trunk. Interestingly the net flow over the cardiac cycle, based on the vessel diameter and the mean velocities, showed a lower correlation to the clinical parameters. Our early results suggest that hepatic hemodynamic analysis at 4D flow MRI may be useful as a biomarker to diagnose early stages of liver cirrhosis and monitor changes in hemodynamics with treatment.

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