Magnetic resonance assessment of the changes associated with portal hypertension in a rat model of portal vein stenosis

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Introduction Portal hypertension is the most important complication of chronic liver diseases and is a leading cause of mortality and liver transplantation worldwide. A characteristic feature of the portal hypertension syndrome is the development of hyperdynamic splanchnic circulation, with an increase in blood flow in splanchnic organs draining into the portal vein and a subsequent increase in portal venous inflow. Such increased portal venous inflow is a significant factor in maintaining and worsening portal pressure elevation. Non-invasive accurate tools for assessing the portal venous inflow are lacking in the clinic [1] and in small animal models despite their usefulness [2,3]. Here we report the determination of alterations in splanchnic blood flow using velocity encoded MRI sequences [1,4] at high field in a rat model of portal hypertension via portal vein stenosis. This portal hypertension model induced structural (vessel diameter) and functional (average blood velocity and volumetric flow rate) perturbations to the abdominal circulation.

Material and methods Adult Wistar rats were anesthetized, the abdomen was opened and the portal vein exposed. Portal vein stenosis was performed by placing a 21-gauge needle on the portal vein. A non-absorbable surgical thread ligature was placed around the vein and needle. The needle was then removed, leaving a calibrated stenosis of the portal vein. Control rats (n = 4) were sham operated. Fifteen (n = 6) and thirty days (n = 5) after the surgical intervention, the animals were subjected to velocity encoded MR phase contrast angiography under gas anesthesia, temperature regulation and respiration rate monitoring. Blood flow in the splenic vein was measured upstream of the stenosis using Fourier flow encoding (flowmap, Bruker, Ettlingen, Germany). Velocity bins of 2.5cm/s were applied, and flow was measured on 10 contiguous 1mm cross-sections of the splenic vein at spatial resolutions of 97μm in-plane. Vessel diameter was evaluated using the lowest velocity bin. Blood velocity was measured, and integrated over the vessel cross-section to yield blood flow. Non parametric Mann-Whitney tests were performed.

Results Typical velocity maps are presented for a control rat and a rat at 15 days after ligature. High velocity bins were more populated in the early stage stenosis than in the late stage, indicating a decrease in blood velocity (figure 1). Quantification (visible on histograms) revealed an increase in vessels diameter (0.93 ± 0.24, 1.27 ± 0.38 and 1.48 ± 0.27 mm at baseline (black boxes), 15 (greyed boxes) and 30 (hashed boxes) days after stenosis, respectively, p < 0.05 at day 30). Besides this morphological change, the hemodynamics were also affected. Average velocity decreased from 4.65 ± 0.74 cm/s at baseline to 3.09 ± 0.48 cm/s or 3.80 ± 1.02 cm/s at 15 and 30 days after stenosis, respectively (p < 0.05 for baseline vs. 15 days). Blood flow of this vessel section increased from 2.46 ± 1.16 ml/min at baseline to 2.90 ± 1.69 ml/min at day 15 (n.s.) and 5.57 ± 2.50 ml/min at day 30 (p < 0.05). Interestingly at late stenosis, the diameter increase was trending towards saturation, yet the flow rate kept increasing, resulting in a slightly increasing velocity.

Conclusions Fourier flow MRI allows an accurate and non-invasive determination of splenic vein diameter and blood flow in rats. The downstream stenosis induced an increase of the diameter, with decreased blood velocity and increased flow. Late stenosis rats had a dramatically increased flow rate, which considering the limited stretching potential of the vessels (indicated by the saturating evolution of vessel diameter), resulted in a slight increase in velocity between days 15 and 30, to a level still below baseline. Assessment of the angiogenic status of the vasculature would however be required for a full understanding of this phenomenon. Nonetheless, this study opens new prospects for non-invasive assessment of splanchnic vascular features at a time when antiangiogenic therapies are used in patients with cirrhosis [5]. These results are in agreement with clinical data in portal hypertension, and suggest our model may be used in the context of pharmacological tests.
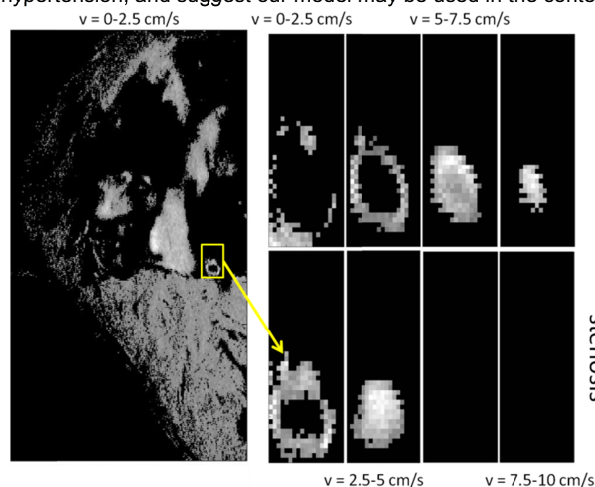

Figure 1: Flow velocity encoded images. Left: overview of the imaged region. Right: presentation of different velocity bins (labeled) for a control (top) and a stenosed (bottom) splenic vein cross-section. Decreased velocity is seen in the stenosed animal.
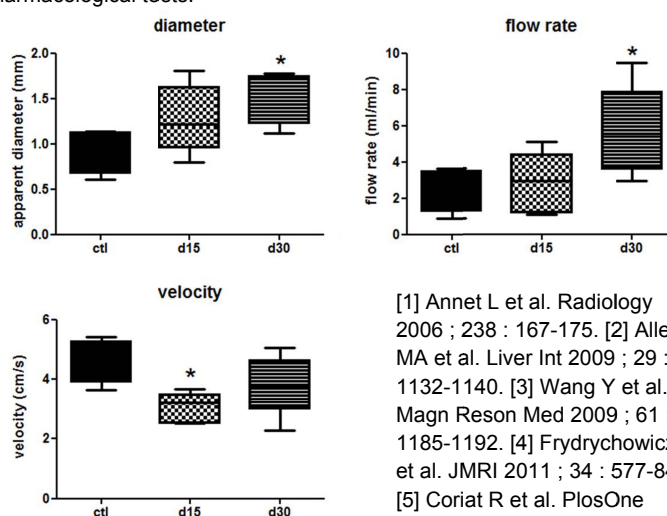

Figure 2: Non-parametric histograms of diameter (upper left), flow rate (upper right) and velocity (lower left) at baseline (black), day 15 (square filling) and day 30 (hashed)post stenosis.

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