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Intrahepatic portal vein blood volume estimated by non-contrast magnetic resonance imaging for the assessment of portal hypertension

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ABSTRACT

Purpose: To investigate the feasibility of estimating the portal vein blood volume that flows into the intrahepatic volume (IHPVBV) in each cardiac cycle using non-contrast MR venography technique as a surrogate marker of portal hypertension (PH).
Materials and methods: Ten patients with chronic liver disease and clinical symptoms of PH (40% males, median age: 54.0, range: 44–73 years old) and ten healthy volunteers (80% males, median age: 54.0, range: 44–66 years old) were included in this study. A non-contrast Triple-Inversion-Recovery Arterial-Spin-Labeling (TIR-ASL) technique was used to quantify the IHPVBV in one and two cardiac cycles. Liver (LV) and spleen volumes (SV) were measured by manual segmentation from anatomical MR images as morphological markers of PH. All images were acquired in a 1.5 T Philips Achieva MR scanner.
Results: PH patients had larger SV ($P = 0.02$) and lower liver-to-spleen ratio ($P = 0.02$) compared with healthy volunteers. The median IHPVBV in healthy volunteers was 13.5 cm^3 and 26.5 cm^3 for one and two cardiac cycles respectively, whereas in PH patients a median volume of 3.1 cm^3 and 9.0 cm^3 was observed. When correcting by LV, the IHPVBV was significantly higher in healthy volunteers than PH patients for one and two cardiac cycles. The combination of morphological information (liver-to-spleen ratio) and functional information (IHPVBV/LV) can accurately identify the PH patients with a sensitivity of 90% and specificity of 100%.
Conclusion: Results show that the portal vein blood volume that flows into the intrahepatic volume in one and two cardiac cycles is significantly lower in PH patients than in healthy volunteers and can be quantified with non-contrast MRI techniques.

1. Introduction

Portal hypertension (PH) is a frequent condition in patients with chronic liver diseases (CLD) and it is characterized by an increased liver resistance to blood flow. The portal vein system is a low pressure system, so this increased resistance induces a rise in the portal pressure gradient (PPG) (Fig. 1A), leading to marked hepatic hemodynamic changes characterized by a decrease in the contribution of portal vein to liver perfusion [1]. The clinical relevance of PH derives from the frequency and severity of its complications, which represent the first cause of hospital admission, death and liver transplantation in patients with cirrhosis [2].

It has been suggested that the severity of PH should be evaluated in all CLD patients as a surrogate measure of the severity of the liver chronic damage and mortality risk, as well as to evaluate the response to treatments [3]. The gold-standard method to measure the portal venous pressure involves an invasive catheterization of

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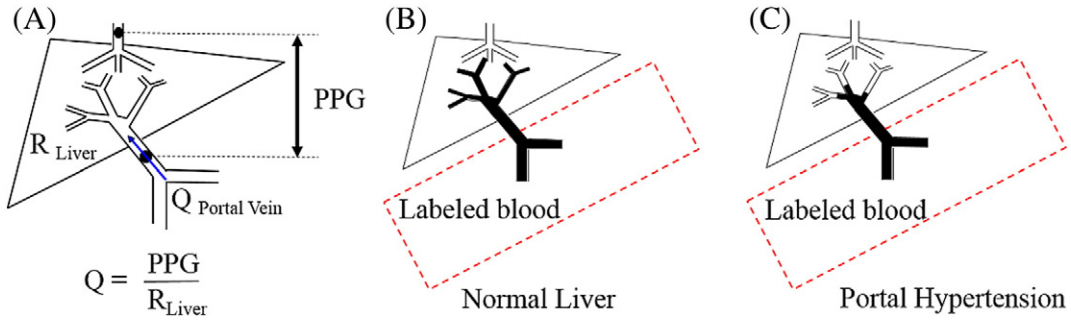

Fig. 1. (A) Schematic representation of the portal vein flow (Q), the liver resistance (R_{Liver}) and the portal pressure gradient (PPG) between the portal vein and the inferior vena cava. (B–C) Expected portal vein blood volume that flows into the intrahepatic volume (IHPVBV) in a certain number of cardiac cycles in a healthy volunteer and a patient with portal hypertension. It is expected that in healthy volunteers the hepatic vascular resistance is low, resulting in larger IHPVBV compared with PH patients.

the cava and hepatic veins, and the measurement of the hepatic venous pressure gradient (HVPG) [3–7]. This method is invasive and uses ionizing radiation, and the need of sedative agents could also modify the hemodynamic response.

Some non-invasive methods to indirectly estimate the HVPG have also been proposed. The arterial enhancement fraction technique (AEF) uses X-ray images to assess the hemodynamic changes associated with diffuse liver disease [8,9], assuming that the AEF indirectly reflects the relationship between arterial perfusion and total (arterial and venous) perfusion [10]. However, this technique requires ionizing radiation and iodinated contrast agent, making it unsuitable for high-risk patients.

A variety of methods based on magnetic resonance imaging (MRI) have also been proposed. Arterial spin labeling (ASL) has been applied to evaluate the liver perfusion in [11–13]. Classical ASL requires a long scanning time when imaging the whole liver due to subject breathing [13]; it is sensitive to motion due to the subtraction step required to suppress the static background, and has low signal-to-noise ratio, producing low-quality images that are not appropriate for quantification. A different approach to estimate the portal vein flow based on MRI phase contrast (PC) technique has also been used [14–19]. Two-dimensional (2D)-PC portal vein flow measurement may not take into account the porto-systemic shunt upstream of the level of measurement [20–22], and could lead to an overestimation of the portal vein blood volume that effectively flows into the liver. Additionally, both the magnetic field inhomogeneities in the abdominal cavity and the need for an accurate definition of the vessels' geometry make it difficult to obtain reliable data using 2D-PC technique. Four-dimensional (4D)-PC portal vein flow technique could take into account the porto-systemic shunt both with [23] and without [24] external contrast agents, but this technique has not been applied to PH patients.

Alternatively, time of flight (TOF) technique has been used to visualize the portal system [25] with the aim of study the liver perfusion. The main drawback of this technique when imaging PH patients is that slow flow does not produce enough signal.

Contrast-enhanced MRI has also been used for hepatic fibrosis grading and staging [26] and to evaluate the portal vein contribution to liver perfusion [27,28]. The radiological sign called "delayed hyperintense portal vein sign" in Gd-EOB-DTPA-enhanced MRI has been proposed as an indirect marker of PH that could reflect the hepatobiliary disease [29]. Two hypotheses have been proposed to explain this sign: one related with the integrity of hepatocytes and the other related with the delay in reaching the intrahepatic space of the contrast agent due to the increased PPG. However, this technique is not routinely used in CLD patients because it requires intravenous contrast agent.

Previously described techniques have not been incorporated into the clinical routine, and PH is still evaluated using morphological changes in the liver and spleen (such as splenomegaly and cirrhosis), and portal vein abnormalities (such as porto-systemic collaterals) [30–32].

In this work a new non-contrast MRI technique is used with the aim of improving PH diagnosis by estimating its effect in the portal vein hemodynamics. We estimated the portal vein blood volume that flows into the intrahepatic volume (IHPVBV) in a certain number of cardiac cycles. The IHPVBV is estimated as a surrogate of the PPG. The rationality of this idea comes from the concept that portal pressure gradient is given by the product of the portal vein flow (Q) and the liver vascular resistance (R_{Liver}) [1] (Fig. 1A), similarly to any vascular system. In PH patients, the labeled blood will face larger vascular resistance to flow into the intrahepatic space, therefore, the IHPVBV is expected to be lower than in healthy volunteers (Fig. 1B–C).

The measurement of the intrahepatic blood volume that flows in a standardized amount of time (e.g. in one or two cardiac cycles) would provide a good estimation of PPG/R_{Liver} and indirectly measures the severity of PH. The proposed method is simple to plan and it is robust to magnetic field (B_0) inhomogeneities.

Table 1
Demographic information and clinical diagnosis of CLD patients include in this study.

No.	Age	Sex	CLD Diagnosis	Clinical signs or symptoms of PH
1	44	F	PBC	Ascites, upper gastrointestinal bleeding
2	49	F	NASH	Ascites, upper gastrointestinal bleeding
3	50	F	NASH	Ascites, upper gastrointestinal bleeding
4	51	F	PBC	Ascites, upper gastrointestinal bleeding
5	53	F	Hepatitis C	Ascites, hepatic encephalopathy
6	54	M	ALD	Ascites, upper gastrointestinal bleeding.
7	56	M	NASH	Ascites, upper gastrointestinal bleeding
8	61	M	NASH	Ascites, upper gastrointestinal bleeding
9	64	M	ALD	Ascites, upper gastrointestinal bleeding
10	73	F	NASH	Ascites, hepatic encephalopathy

NASH: Nonalcoholic steatohepatitis; PBC: Primary biliary cirrhosis; ALD: Alcoholic liver disease.