A novel noninvasive assessment of hepatic venous pressure gradient and portal pressure computed from computed tomography angiography

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Cirrhosis is a severe and common digestive disease worldwide and is associated with a poor outcome. Portal hypertension (PHT) is a frequently encountered complication in cirrhotic patients [1–3]. Therefore, evaluation of portal pressure (PP) is urgently needed for the grading and staging of PHT. Direct measurement of PP is rarely performed due to significant invasiveness and potential complications. Hepatic venous pressure gradient (HVPG) is currently treated as the "gold standard" [1–4]. However, the invasiveness and technical difficulty greatly restrict its repeatable application.

An index computed from computed tomography angiography (CTA) has recently demonstrated its diagnostic value compared with the "gold standard" [5, 6]. For instance, fractional flow reserve from coronary CTA showed good performance in the diagnosis of functional coronary stenosis in a multicenter randomized clinical controlled trial on 159 vessels in 103 patients [6]. On the basis of our previous study of noninvasive measurement of coronary stenosis by fractional flow reserve [7], this study, for the first time, introduces a novel noninvasive assessment of HVPG ($HVPG_{ni}$) and PP (PP_{ni}) computed from three dimensional (3D) hepatic portal venous models reconstructed from CTA to diagnose the severity of PHT in cirrhotic patients.

The patient enrolled in the pilot study was a 50-year-old man who showed visible clinical manifestations of PHT, such as ascites and splenomegaly, and was diagnosed with cirrhosis in the decompensated stage. Approval was obtained from the ethical committees of Tongji Hospital and the participant gave written informed consent in advance.

The CTA was performed with multi-detector CT scanners (GE LightSpeed Ultra, 120 kV, 220 mA). Original images were spilt into thin layers and exported into imaging control software MIMICS10.0. 3D hepatic portal venous models were reconstructed from surrounding tissues by different CT values, which were then meshed with 3D Flotran elements in the software ANSYS11.0. Given boundary conditions including average velocity of hepatic venous and portal venous flow were measured by color Doppler ultrasound (CDUS) (Philips iU22 x MATRIX Ultrasound System,

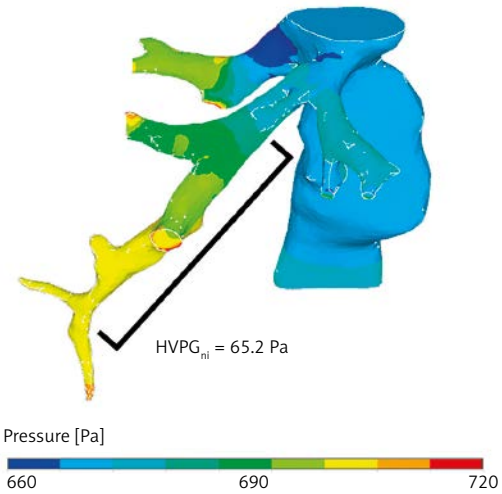

Figure 1. Noninvasive assessment of hepatic venous pressure gradient in decompensated cirrhosis. Hepatic venous pressure gradient was calculated *in vitro* with the value of 65.2 Pa

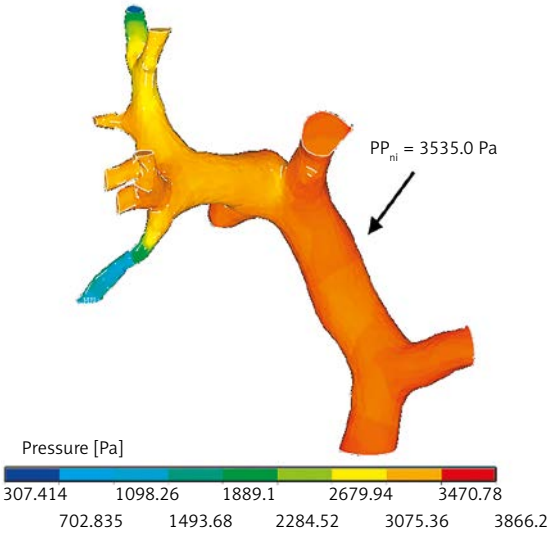

Figure 2. Noninvasive assessment of portal pressure in decompensated cirrhosis. Portal pressure was quantified *in vitro* as 3535.0 Pa and was generally consistent with the clinical diagnosis of portal hypertension

convex array probe C5-2). Afterwards, finite element analysis and computational fluid dynamics were applied to compute the pressure distribution in the hepatic portal vein *in vitro*.

Clinical data of the decompensated cirrhotic patient were calculated to test the feasibility and accuracy of the novel noninvasive assessment with the clinical diagnosis, CTA and CDUS as reference standards. The CTA images showed that the diameter of the portal vein was 1.6 cm while the normal diameter is ≤ 1.3 cm [2, 3]. Besides, the average velocity of portal venous flow was 12.5 cm/s, which was obviously slower than 22.62 cm/s in normal patients [1, 3, 4] and indicated severe PHT. According to the calculation by the novel assessment, HVPG$_{ni}$ and PP$_{ni}$ were computed as 65.2 Pa (Figure 1) and 3535.0 Pa (Figure 2), which generally corresponded to the diagnosis of PHT. Furthermore, the pressure and velocity distribution of different sections could be simultaneously obtained.

The PHT is known as a frequent complication of cirrhosis worldwide which significantly reduces the patient's quality of life. The HVPG is currently considered as the "gold standard" to identify PHT. However, shortcomings, such as invasiveness and technical difficulty, limit its diagnostic worth greatly.

In the pilot study, finite element analysis and computational fluid dynamics over the 3D hepatic portal venous model were applied, which potentially developed a novel noninvasive assessment of HVPG$_{ni}$ and PP$_{ni}$ to evaluate the severity of PHT. Besides, the novel assessment was successfully applied and the diagnostic performance of HVPG$_{ni}$ and PP$_{ni}$ was overall consistent with the clinical diagnosis, CTA and CDUS.

This study introduces, for the first time, a novel noninvasive assessment of HVPG$_{ni}$ and PP$_{ni}$ computed from hepatic portal venous models, which might be a potential diagnostic tool to evaluate the severity of PHT, grading of cirrhosis and choice of treatment in the future. However, large randomized clinical controlled trials evaluated by both the novel assessment and invasive "gold standard" are needed before the application from bench to bedside.

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