Editorial Commentary

Subharmonic scattering of ultrasound contrast agent microbubbles may be an effective and promising tool for portal vein pressure estimation

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Portal hypertension (PH) is a commonly observed syndrome in patients with cirrhosis and other chronic liver diseases (1). It is closely associated with severe clinical complications, including upper gastrointestinal hemorrhage, ascites, hepatic encephalopathy, and liver failure (2-6). Portal vein pressure (PVP) is a prognostic indicator for patients with cirrhosis, and PH is a contraindication for hepatectomy (7,8). Currently, the gold standard for assessing PVP is the measurement of PVP gradient [hepatic venous pressure gradient (HVPG)], which is indirectly determined by placing a catheter in the hepatic vein (3). However, the invasive nature of this procedure and the associated risks of bleeding, bile leakage, and infection restrict its clinical applicability (9,10). Hence, there is an urgent need to develop a non-invasive method for accurately measuring PVP, catering to the demand for close clinical monitoring of PVP.

In recent years, advancements in ultrasound contrast agent microbubbles and imaging technology have opened up possibilities for non-invasive hemodynamic monitoring. Ultrasonic contrast agent microbubbles are composed of a gas core surrounded by a lipid or polymer shell. These microbubbles exhibit changes in size and acoustic properties in response to ambient pressure variations, owing to its compressibility (11). Leveraging this characteristic, a novel technology known as subharmonic-aided pressure estimation (SHAPE) has emerged, which utilizes ultrasound contrast agents (such as SonoVue and Sonazoid) as pressure sensors. SHAPE relies on the correlation between microbubble subharmonics and ambient pressure, enabling non-invasive assessment of blood pressure (12). This innovative technology has garnered significant attention and is currently undergoing in-depth research. In a study conducted by Eisenbrey *et al.* (13), the SHAPE gradient between the portal vein and hepatic vein was compared with HVPG measurement. The findings indicated a generally good agreement between the two, suggesting that the SHAPE technique holds potential as a valuable tool for diagnosing clinical PH. Another clinical study involving 125 patients, which measured PVP using Sonazoid microbubbles, revealed consistent results between the SHAPE gradient and HVPG measurements (14). This suggests that SHAPE could be a promising technique for non-invasive detection of PH.

In recent years, there has been significant advancement in the estimation of PVP using the SHAPE technique. Xu *et al.* (15) conducted *in vitro* simulation experiments utilizing two confocal single element transducers. The results revealed that the subharmonic scattering of SonoVue microbubbles exhibited three stages: the first growth stage (40–300 kPa), saturation (300–400 kPa), and the second growth stage (400–540 kPa). The second growth stage was found to be more suitable for measuring lower ambient pressures. At a high incident acoustic pressure of 520 kPa, there was a strong correlation between subharmonic amplitude and ambient pressure. Lu *et al.* (16) established

a PH model using two dogs and demonstrated a linear correlation between subharmonic amplitude and PVP (<20 mmHg) at an incident acoustic pressure of 453 kPa. *In vivo* experiments conducted by Xu *et al.* using canine models of PH further validated these findings. They reported high sensitivity, specificity, and accuracy rates of 93.3%, 91.7%, and 92.6%, respectively, in diagnosing PH when the incident acoustic pressure was set at 563 kPa (17). These experimental findings indicate that the subharmonic scattering of ultrasonic contrast agent microbubbles offers a promising non-invasive method for assessing PVP.

While the existing *in vitro* simulation experiments and animal studies have yielded promising outcomes, addressing the challenges posed by attenuation through various human tissues and the heterogeneity among clinical patients remains an urgent concern. Furthermore, optimizing experimental parameters to enhance the sensitivity and accuracy of SHAPE technology in estimating PVP represents a significant current challenge. Additionally, large-scale clinical studies are necessary to validate the feasibility and clinical value of utilizing SonoVue microbubbles as non-invasive sensors for PVP estimation.

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Footnote

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