

## Contrast-enhanced ultrasound in portal venous system aneurysms: A multi-center study

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### Abstract

**AIM:** To investigate contrast-enhanced ultrasound (CEUS) findings in portal venous system aneurysms (PVSA).

**METHODS:** In this multi-center, retrospective, case series study, we evaluated CEUS features of seven cases of PVSA that were found incidentally on conventional ultrasound in the period 2007-2013. Three Ultrasound Centers were involved (Chieti, Italy, Bad Mergentheim, Germany, and Cluj-Napoca, Romania). All patients underwent CEUS with Sonovue® (Bracco,

Milan, Italy) at a standard dose of 2.4 mL, followed by 10 mL of 0.9% saline solution. The examinations were performed using multifrequency transducers and low mechanical index. We considered aneurysmal a focal dilatation of the portal venous system with a size that was significantly greater than the remaining segments of the same vein, and that was equal or larger than 21 mm for the extrahepatic segments of portal venous system, main portal vein and bifurcation, and 9 mm for the intrahepatic branches.

**RESULTS:** After contrast agent injection, all PVSA were not enhanced in the arterial phase (starting 8-22 s). All PVSA were then rapidly enhanced in the early portal venous phase (starting three to five seconds after the arterial phase, 11-30 s), with persistence and slow washout of the contrast agent in the late phase (starting 120 s). In all patients, CEUS confirmed the presence of a "to-and-fro" flow by showing a swirling pattern within the dilatation in the early portal venous phase. CEUS also improved the delineation of the lumen, and was reliable in showing its patency degree and integrity of walls. In one patient, CEUS showed a partial enhancement of the lumen with a uniformly nonenhancing area in the portal venous and late phases, suggesting thrombosis.

**CONCLUSION:** In our case series, we found that CEUS could be useful in the assessment and follow-up of a PVSA. Further studies are needed to validate its diagnostic accuracy.

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**Key words:** Venous system; Portal vein; Aneurysm; Contrast-enhanced ultrasound; Computed tomography; Magnetic resonance imaging

**Core tip:** Portal venous system aneurysms (PVSA) are considered a rare disease. Ultrasound is the method of choice in the initial assessment of a suspected PVSA,

by showing a focal enlargement of the portal venous system with typical color Doppler features. However, no studies have so far reported contrast-enhanced ultrasound (CEUS) findings. In this multi-center, retrospective, case series study we demonstrated, for the first time, that CEUS could be useful in the assessment and follow-up of a PVSA.

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## INTRODUCTION

Portal venous system aneurysms (PVSAs) are considered a rare disease, representing 3% of all venous aneurysms. However, their prevalence varies among published studies, reflecting the different imaging techniques used (0.6-4.3 per 1000 patients)<sup>[1,2]</sup>. These lesions remain often underdiagnosed due to their asymptomatic course, but their identification is important to choose an appropriate treatment in complicated cases or to follow-up asymptomatic ones over time. Furthermore, an incidental PVSA could be suggestive of an underlying disease that may require specific therapy<sup>[1]</sup>. The first case was reported by Barzilai *et al*<sup>[3]</sup> in 1956. Ultrasound is the method of choice in the initial assessment of a suspected PVSA, by showing a focal enlargement of the portal venous system with typical color Doppler features. The role of computed tomography (CT) and magnetic resonance imaging (MRI) is also established<sup>[1]</sup>. However, no studies have so far reported contrast-enhanced ultrasound (CEUS) findings. In the last decade, CEUS has become commonly used in clinical practice. Since its first use to differentiate malignant from benign focal liver lesions, other clinical applications have been carried out, as supported by several controlled studies. In comparison to CT and MRI, CEUS demonstrates several advantages, such as the absence of radiation exposure and of the use of nephrotoxic contrast agents. Furthermore, CEUS allows real-time evaluation of disease, which cannot be performed with traditional imaging<sup>[4-6]</sup>. In view of these several advantages and the lack of evidence for PVSAs, the aim of this study was to investigate the role of CEUS in the patients affected.

## MATERIALS AND METHODS

In this multi-center, retrospective, case series study, we evaluated CEUS findings in seven cases of PVSAs that were found incidentally on conventional ultrasonography in the period 2007-2013. Three Ultrasound Centers were involved (Chieti, Italy, Bad Mergentheim, Germany, and Cluj-Napoca, Romania). Data regarding age, sex, medical

history and outcome of the patients and B-mode, color Doppler ultrasound (CDUS) and CEUS findings of the lesions were all recorded. All patients underwent CEUS with Sonovue® (Bracco, Milan, Italy) at a standard dose of 2.4 mL, followed by 10 mL of 0.9% saline solution. The examinations were performed using multi-frequency transducers and low mechanical index (MI).

There is no consensus on the definition of PVSAs, and we considered aneurysmal, according to current knowledge, a dilatation of the portal venous system with a size that was significantly greater than the remaining segments of the same vein, and that was equal or larger than 21 mm for the extrahepatic segments of portal venous system, main portal vein (PV) and bifurcation, and 9 mm for the intrahepatic branches of the PV<sup>[1]</sup>. Written informed consent was obtained from each subject.

Clinical, B-mode and CDUS findings are summarized in Table 1. All patients had a single portal venous system aneurysm. PVSA was located in the extrahepatic portal venous system in two patients (patients 1 and 2, extrahepatic segment of main PV and splenomesenteric confluence, Figures 1 and 2, respectively). Furthermore, the PVSA was located in the left and right main branches of PV in four patients (patient 3, Figure 3 in the left, and patient 4, 5, Figure 4, in the right main branch of portal vein). In one patient, PVSA was located in the pars umbilicalis.

PVSAs had a saccular configuration in two patients (3 and 5, Figures 3 and 4, respectively). In the other patients, PVSAs had a fusiform configuration. The maximum size ranged between 22 and 37 mm (median, 25 mm). CDUS revealed a “to-and-fro” flow signal in 6/7 patients, with a clear “Yin-Yang” sign only in patient 3 (Figure 3). In patient 2, B-mode US demonstrated a slightly echogenic area within the dependent portion of the lumen. CDUS revealed turbulent flow with mosaic color only within a portion of portal lumen (Figure 2). In all patients, spectral analysis revealed portal venous flow.

## RESULTS

The CEUS findings of PVSAs in our case series are summarized in Table 2. After contrast agent injection (Figures 1-4), all PVSAs were not enhanced in the arterial phase (starting 8-22 s<sup>[4-6]</sup>). Then, all PVSAs were rapidly enhanced in the early portal venous phase (starting three to five seconds after the arterial phase, 11-30 s), with persistence and slow washout of the contrast agent in the late phase (starting 120 s). In all patients, CEUS confirmed the presence of a “to-and-fro” flow by showing a swirling pattern within the dilatation in the early portal venous phase.

In all patients, CEUS improved the delineation of the lumen and was reliable in showing the integrity of walls, by excluding contrast extravasation from the lesions. Furthermore, CEUS successfully documented the degree of patency of the lumen. In 6/7 patients, CEUS showed complete enhancement of the lesions in the early portal

**Table 1 Clinical, B-mode and color Doppler ultrasound findings of portal venous system aneurysms**

No.	Patient		Indication for first US examination	Medical history	US device	B-mode and CDUS findings						
	Sex	Age (yr)				PVSAs (n)	Location	Configuration (mm)	Features	Others	2 <sup>nd</sup> imaging	Outcome
1	F	56	Suspected NAFLD	Overweight, dyslipidemia	GE Logiq S8, convex probe	1	Main portal vein, extrahepatic segment	Fusiform/30	Patent lumen, to-and-fro flow	Fatty liver	CEUS	12-mo follow-up with B-mode and CDUS
2	M	65	Upper GI bleeding from grade III esophageal varices	Alcoholic cirrhosis	GE Logiq E9, convex probe	1	Splenomesenteric confluence	Fusiform/37	Lumen partially filled with a slightly echogenic area, without flow on CDUS; turbulent flow with mosaic color within patent lumen	Cirrhotic liver	CEUS, CECT	Anticoagulation and 12-mo follow-up with B-mode and CDUS
3	M	64	Dyspepsia	Gastritis treated with omeprazole	Aloka prosound, convex probe	1	V segment, left main branch of portal vein	Saccular/22	Patent lumen, to-and-fro flow ("Yin-Yang" sign)	None	CEUS, CECT	At a 6-mo follow-up: increase in size with US; no complications with CEUS
4	F	80	Follow-up surveillance after surgical removal of colon cancer 7 years before	Type 2 diabetes treated with insulin	Aloka prosound, convex probe	1	Right main branch of portal vein	Fusiform/23	Patent lumen, to-and-fro flow	Small bilateral renal cysts	CEUS	12-mo follow-up with B-mode and CDUS
5	M	58	Elevated liver function tests	None	Acuson Sequoia, convex probe	1	Right main branch of portal vein	Saccular/25	Patent lumen, to-and-fro flow	None	CEUS	12-mo Follow-up with B-mode and CDUS
6	F	38	Elevated liver function tests	HIV	Acuson Sequoia, convex probe	1	Pars umbilicalis	Fusiform/32	Patent lumen, to-and-fro flow	None	CEUS, CECT	12-mo follow-up with B-mode and CDUS
7	M	62	Weight loss	Vasculitis	Acuson Sequoia, convex probe	1	Right main branch of portal vein	Fusiform/23	Patent lumen, to-and-fro flow	None	CEUS	12-mo follow-up with B-mode and CDUS

CEUS: Contrast-enhanced ultrasound; CECT: Contrast-enhanced computed tomography; CDUS: Color Doppler ultrasound; HIV: Human immunodeficiency virus.

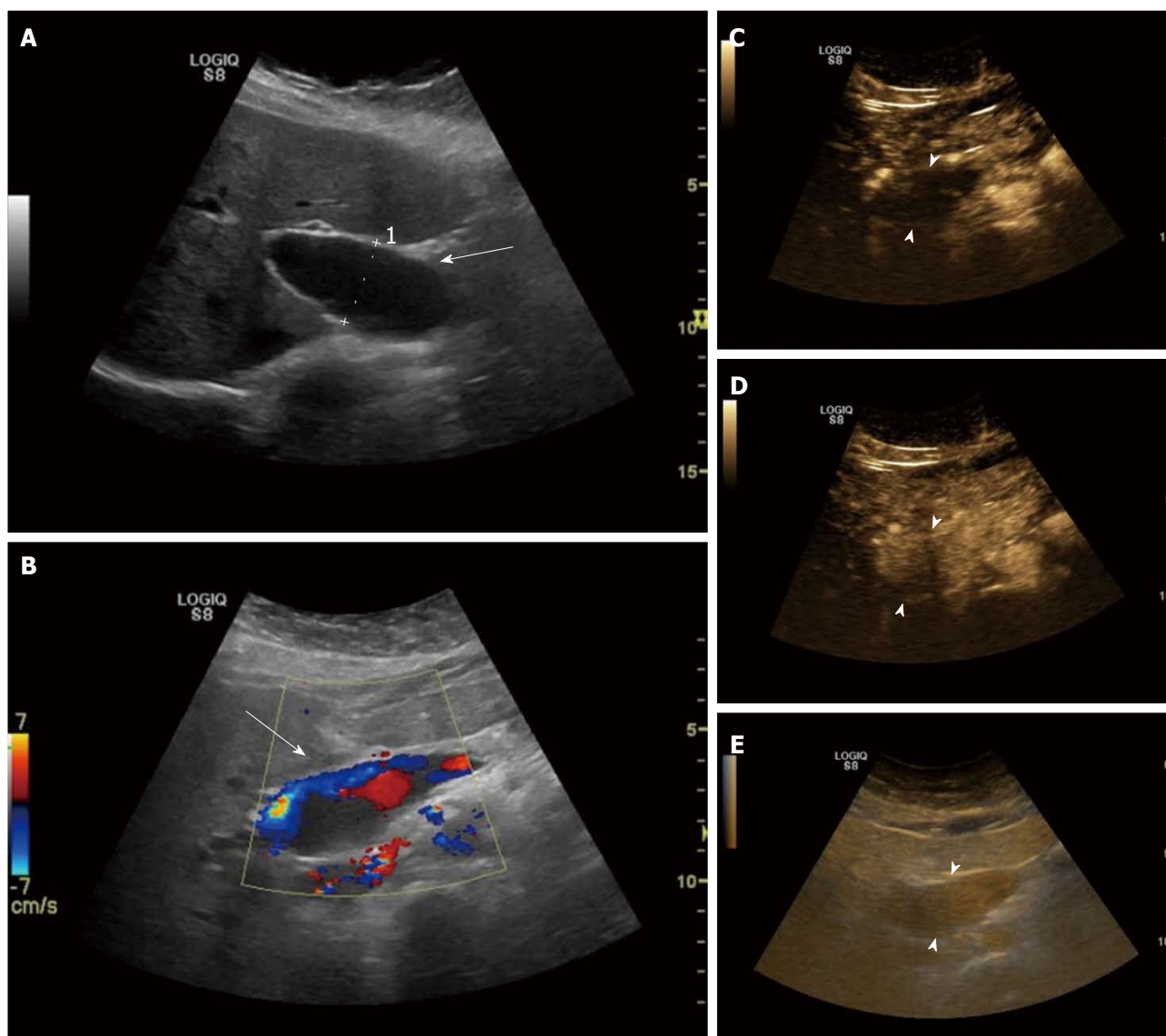
venous phase. In patient 2, a partial enhancement of the lumen was documented with a uniformly non-enhancing area in the portal venous and late phases, suggesting thrombosis. These findings were confirmed by contrast-enhanced CT (CECT, Figure 2).

In patient 3, CEUS was useful also in the follow-up: at six months, CEUS was repeated because of a slight increase in size of the PVSA (2.6 cm), and it successfully excluded further complications, such as thrombosis and fistulas (Table 1).

## DISCUSSION

The origin of PVSAs may be congenital or acquired. The first may arise from defective regression of the right primitive vitelline vein or from wall vein weakness, and their inherent condition is suspected on the basis of the absence of acquired risk factors, such as trauma

or diseases (*e.g.*, hepatocellular carcinoma, liver cirrhosis or pancreatitis)<sup>[7-9]</sup>. A unique case of a giant congenital aneurysm of the PV associated with peliosis hepatis and intestinal lymphangiectasia has been reported in the literature<sup>[10]</sup>. Some PVSAs have been described in association with hereditary hemorrhagic telangiectasia<sup>[11,12]</sup>. Acquired cases are most commonly associated with portal hypertension secondary to chronic liver disease, which leads to intimal thickening, compensatory hypertrophy of the tunica media and weak fibrous tissue replacement, predisposing to the formation of the aneurysm<sup>[1,13]</sup>. In the case of association with pancreatitis or with trauma or previous surgical intervention, some authors have instead hypothesized that inflammation or injury, respectively, could weaken the vessel walls, thus leading to aneurysmal dilatation<sup>[14,15]</sup>. PVSAs are usually located in extrahepatic segments of the portal venous system, such as splenomesenteric confluence and main PV.



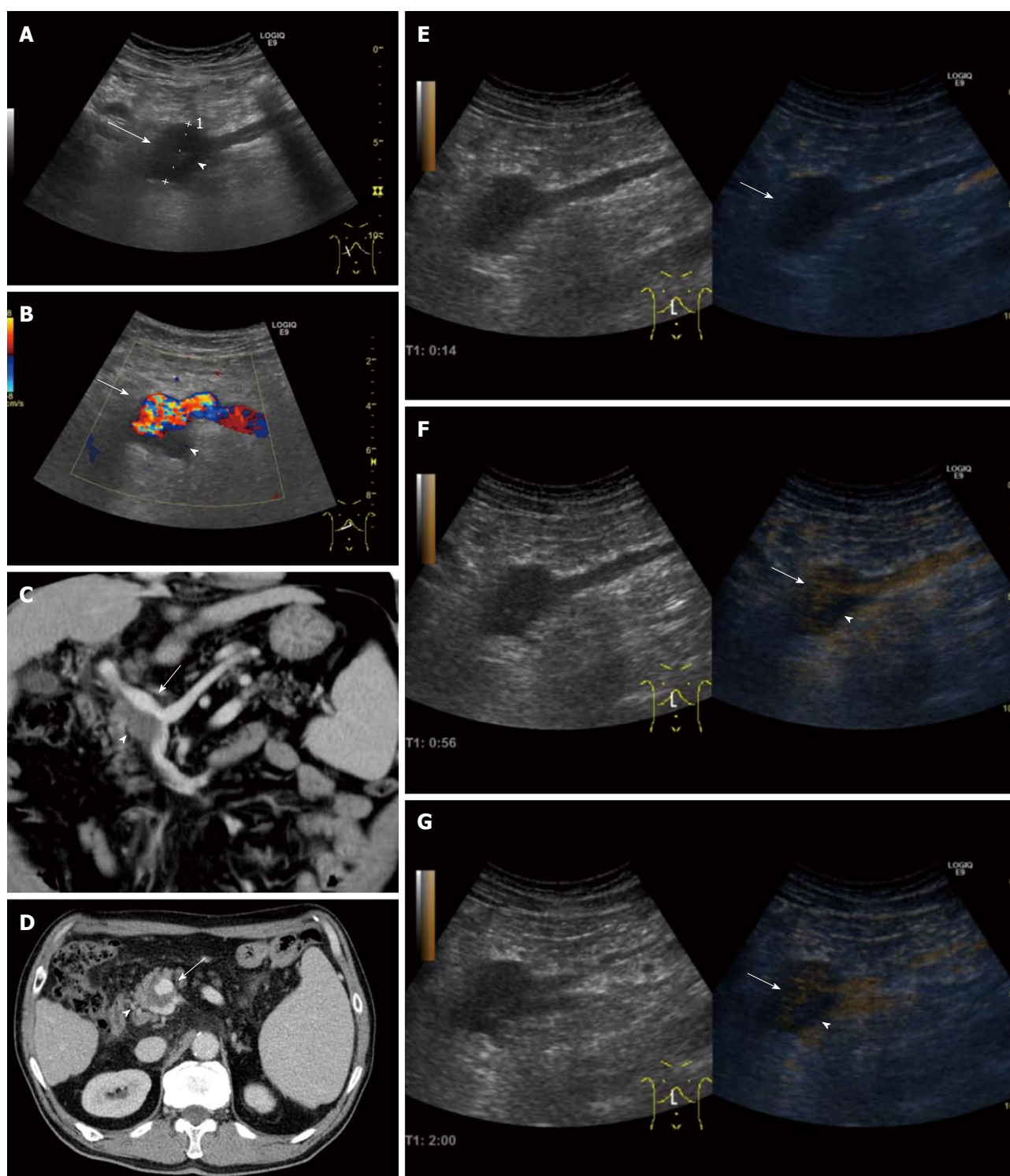
**Figure 1** Patient 1: Portal venous system aneurysm in a 56-year-old woman with a history of overweight and dyslipidemia, who was referred because of suspected nonalcoholic fatty liver disease. A: Right oblique sagittal view shows a focal fusiform dilatation of the extrahepatic segment of the main portal vein (arrow), with a maximum diameter of 30 mm (caliper 1); B: Right oblique sagittal view with color Doppler shows “to-and-fro” flow signal inside the lesion (arrow); C: Right oblique sagittal view shows the contrast-enhanced ultrasound characteristics of the portal venous system aneurysm which is not enhanced in the arterial phase (17 s, arrowheads); D: Homogenously enhanced throughout the early portal venous phase (22 s, arrowheads); E: Persistently enhanced with slow washout in the late phase (301 s, arrowheads).

Rarely, they affect splenic, mesenteric, and paraumbilical veins<sup>[16,17]</sup>. PVSAs are sometimes associated with an unusual tortuosity of the portal vein; this phenomenon has been attributed to hemodynamic changes in the portal venous system<sup>[18]</sup>. PVSAs are usually asymptomatic and found incidentally, and symptoms (*e.g.*, abdominal pain) are more frequently associated with thrombosed, multiple and/or larger aneurysms<sup>[1]</sup>. Rarely, PVSAs are associated with complications such as arteriportal fistulas, rupture, gastrointestinal bleeding, inferior vena cava obstruction and duodenal and biliary compression, the latter associated with cholestasis<sup>[19-23]</sup>. Surgical treatment should be considered when the aneurysms expand and symptoms or complications arise<sup>[24]</sup>.

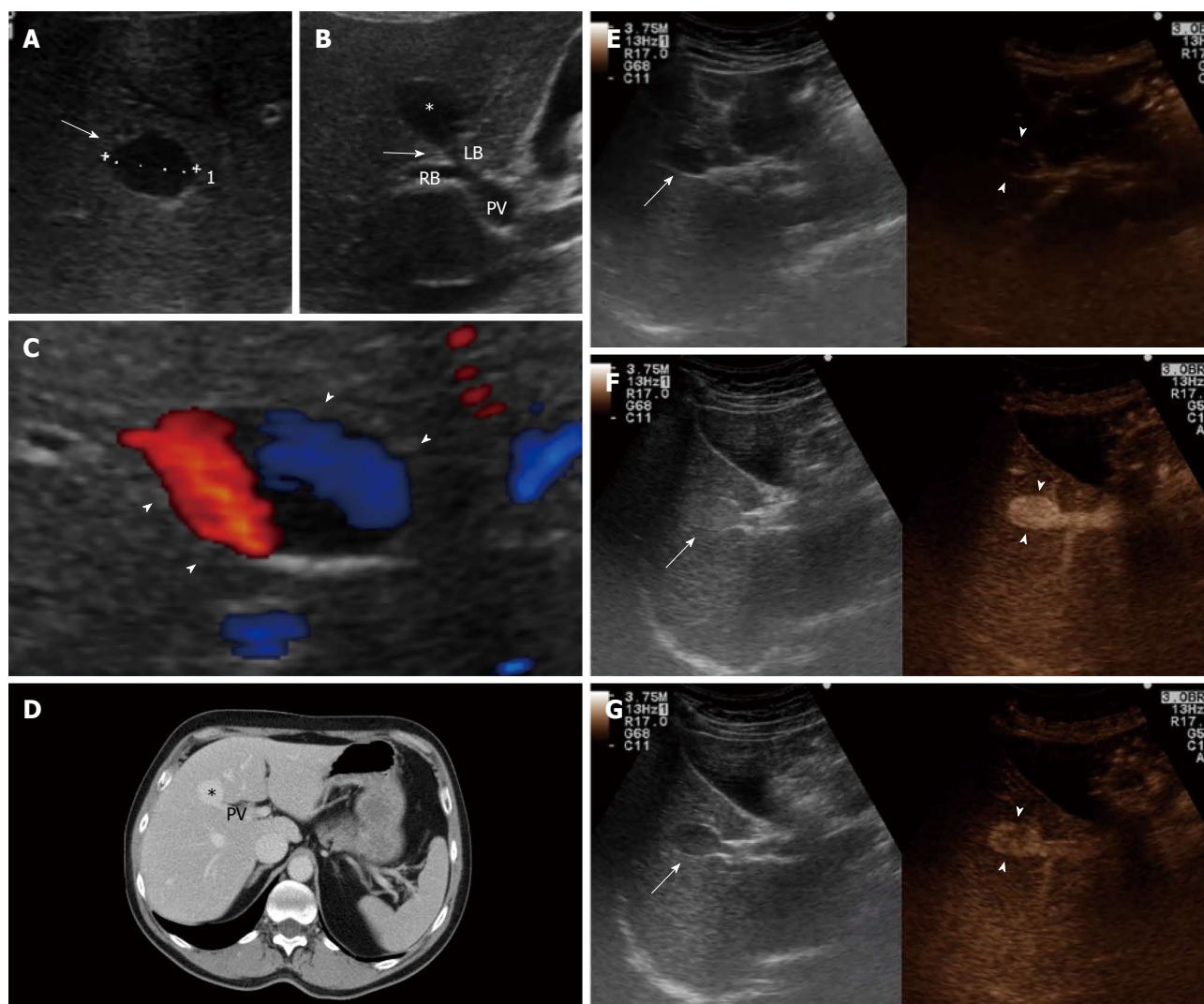
Ultrasound is the method of choice in the initial

assessment of a PVSA, reserving other imaging techniques (*e.g.*, CT and MRI) for indeterminate US or when a complication is suspected<sup>[1]</sup>. B-mode US can reveal an anechoic lesion in contiguity with the main PV or its branches, and it can correctly estimate size, lumen and wall characteristics<sup>[25-27]</sup>. Use of color Doppler US improves the visualization of patency of lumen and flow characteristics; the finding of a “to-and-fro” flow signal (“Yin-Yang” sign, as blood flows in and out during systole and diastole, respectively) can be highly suggestive of an abnormal vessel dilatation; spectral analysis reveals a portal venous flow inside the lesion (nonpulsatile monophasic waveform), thus confirming its origin in the portal venous system<sup>[28,29]</sup>. US has also proved to be effective in the assessment of complications such as





**Figure 2** Patient 2: Portal venous system aneurysm in a 65-year-old man with a history of alcoholic liver cirrhosis, who presented with hematemesis secondary to rupture of esophageal varices (grade III), which were successfully treated with endoscopic ligation. A: Right oblique sagittal view shows a focal fusiform dilatation of the portal venous system at the splenomesenteric confluence (arrow), with a maximum diameter of 37 mm (caliper 1) and lumen partially filled with a slightly echogenic area (arrowhead); B: Right oblique transverse view with color Doppler shows turbulent flow with mosaic color within patent lumen (arrow) and absence of flow within echogenic area (arrowhead); C-G: Contrast-enhanced ultrasound (CEUS) and computed tomography (CT) findings: Right oblique sagittal view shows the CEUS characteristics of the portal venous system aneurysm (PVSA), which is not enhanced in the arterial phase (14 s, arrow, E) and partially hyperenhancing through the portal venous (56 s, arrow, F) and late phase (2 min, arrow, G), with a persistent non-enhancing area in both phases (arrowheads), suggestive of incomplete appositional thrombosis of the PVSA. Axial (D) and coronal maximum intensity projection CT (C) images show the fusiform aneurysm during the portal venous phase, without enhancement in its dependent portion, confirming the diagnosis of partially thrombosed PVSA.



**Figure 3** Patient 3: Portal venous system aneurysm in a 64-year-old man who presented with a 3-mo history of dyspepsia. A: Right transverse subcostal view shows an anechoic lesion without posterior acoustic enhancement in the hepatic segment V (arrow), with a maximum size of 22 mm (caliper 1); B: Right oblique sagittal view shows the direct communication between the lesion (asterisk) and the left branch of the portal vein (arrow); C: Right transverse subcostal view with color Doppler shows "to-and-fro" flow inside the lesion ("Yin-Yang" sign, arrowheads); D-G: Contrast-enhanced ultrasound (CEUS) and computed tomography (CT) findings: Right oblique sagittal view, in dual screen mode, shows the CEUS characteristics of the portal venous system aneurysm (PVSA) (arrows), which is not enhanced through the arterial phase (8 s, arrowheads, E) and completely hyperenhanced with a swirling pattern throughout the portal venous phase (1 min 7 s, arrowheads, F). The PVSA is evident also during the late phase (2 min 28 s, arrowheads, G). Axial CT scan (D) confirmed the presence of sacciform PVSA (asterisk) during the portal phase. PV: Portal vein; RB and LB: Right and left branches of the portal vein, respectively.

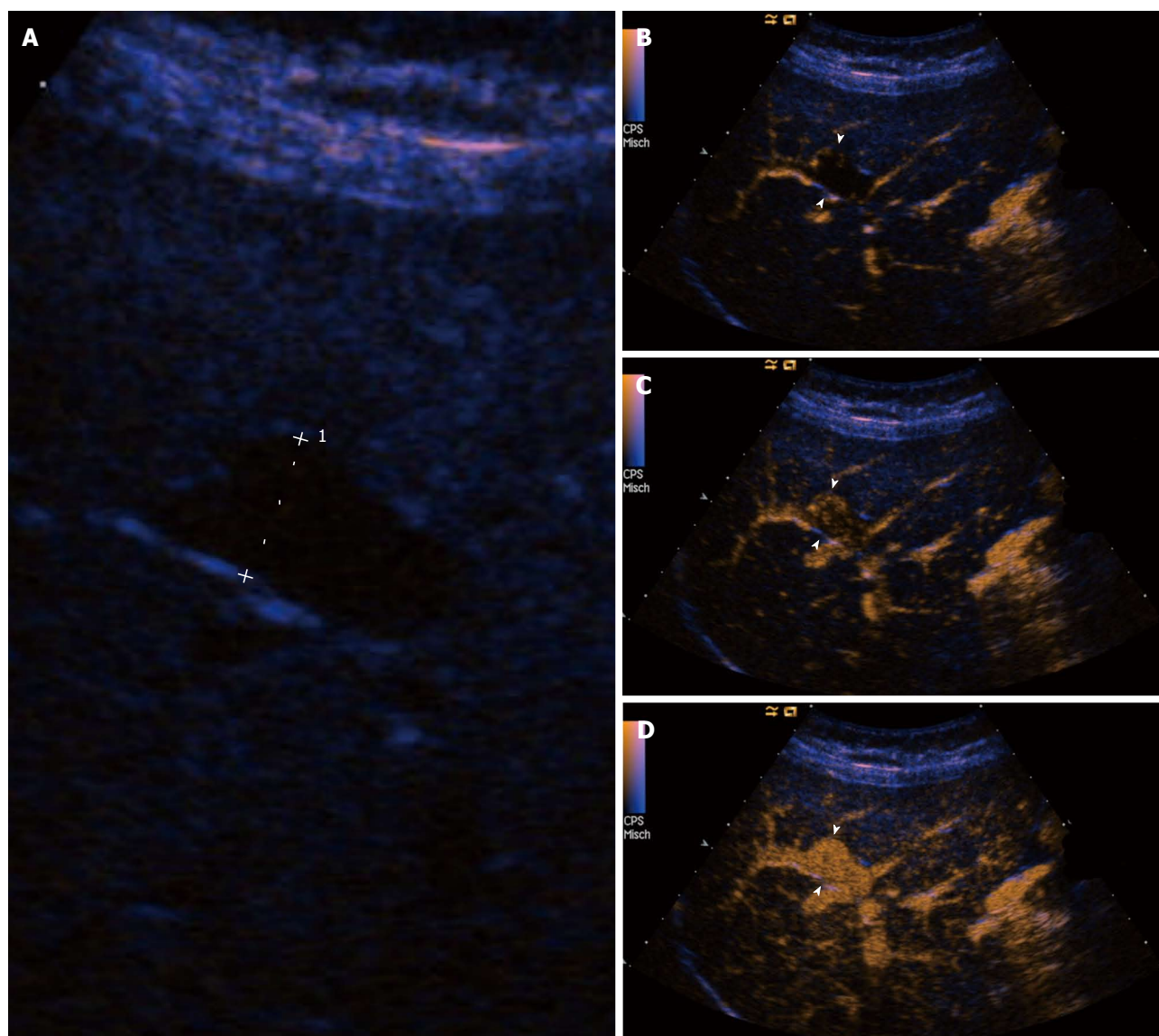
thrombosis, by showing echoes inside the lumen and absence of flow on CDUS<sup>[30]</sup>.

To the best of our knowledge, however, no CEUS pattern for PVSAs has so far been described in the literature. Because of the rarity of the disease, a multi-center study was designed. In our case series, CEUS overcame some limitations of B-mode and CDUS in the assessment of a PVSA. CEUS improved the delineation of the lumen and correctly documented the patency degree and integrity of the walls. Furthermore, CEUS confirmed the correct configuration of the PVSA (fusiform or saccular) and the presence of a "to-and-fro" flow signal by showing a swirling pattern within the aneurysm, a dynamic sign that cannot be demonstrated on CT and MRI, because of their static modality of acquisition of images, and that confirms the presence of

abnormal flow within the dilatation. CEUS has already demonstrated high sensitivity and specificity in the diagnosis of the nature of PV thrombosis in the non-aneurysmal portal vein<sup>[31-33]</sup>; in our case series, CEUS was effective to confirm the diagnosis of incomplete PV thrombosis in a patient with PVSA, and successfully revealed its benign nature.

Catalano *et al.*<sup>[34]</sup> have previously documented the usefulness of CEUS to reveal a peripheral arteriportal fistula, by showing a transient area of hyperechogenicity during the arterial phase, with early opacification of peripheral portal branches. In our case series, the absence of early arterial enhancement, and the absence of visualization of abnormal communication with other vessels, excluded complications such as arteriportal fistulas, as confirmed by CECT in two patients. The use





**Figure 4 Patient 5: Portal venous system aneurysm in a 58-year-old man who was referred because of elevated liver function tests.** A: Right transverse subcostal view shows a focal saccular dilatation of the right main branch of the portal vein, with a maximum diameter of 25 mm (caliper 1); B-D: Right transverse subcostal view shows the contrast-enhanced ultrasound characteristics of the portal venous system aneurysm (PVSA), which is not enhanced in the arterial phase (16 s, arrowheads, B) and starts to enhance through the early portal venous phase (18 s, arrowheads, C). The PVSA is completely enhanced during portal venous phase (21 s, arrowheads, D).

of CEUS can be particularly advantageous in patients with kidney damage, because ultrasound contrast agents are not nephrotoxic, and their use is safe without any need of premedication and laboratory tests before starting contrast examination<sup>[4]</sup>. CEUS was also reliable in the follow-up of a patient. Though US documented a slight increase in size in patient 3 at a 6-mo follow-up, no surgical treatment was performed because the patient remained asymptomatic and no complications were found on check-up with CEUS. The absence of radiation exposure avoids unnecessary biological risk in patients undergoing follow-up, and examinations could be repeated over time with a better cost-effectiveness profile than other imaging techniques, such as CT<sup>[4]</sup>. In conclusion, in our case series, we found that CEUS could be useful in the assessment

and follow-up of a PVSA. However, before considering CEUS as an alternative method to traditional imaging, such as CT or MRI, further studies are needed to validate its diagnostic accuracy.

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**Table 2 Contrast-enhanced ultrasound findings of portal venous system aneurysms**

Patient No.	Contrast agent and dose	Arterial phase	Portal venous phase	Late phase	Final diagnosis
1	Sonovue, 2.4 mL	No enhancement	Enhancement	Enhancement with slow washout	Fusiform PVSA
2	Sonovue, 2.4 mL	No enhancement	Partial enhancement of the lumen with uniformly nonenhancing area	Partial enhancement of the lumen with slow washout; persistent non-enhancing area	Fusiform PVSA complicated by incomplete benign thrombosis
3	Sonovue, 2.4 mL	No enhancement	Enhancement	Enhancement with slow washout	Saccular PVSA
4	Sonovue, 2.4 mL	No enhancement	Enhancement	Enhancement with slow washout	Fusiform PVSA
5	Sonovue, 2.4 mL	No enhancement	Enhancement	Enhancement with slow washout	Saccular PVSA
6	Sonovue, 2.4 mL	No enhancement	Enhancement	Enhancement with slow washout	Fusiform PVSA
7	Sonovue, 2.4 mL	No enhancement	Enhancement	Enhancement with slow washout	Fusiform PVSA

PVSA: Portal venous system aneurysm.

## COMMENTS

### Background

Portal venous system aneurysms (PVSA) are often underdiagnosed, due to their asymptomatic course, and found incidentally on conventional imaging. Unenhanced ultrasound (US) (B-mode and color Doppler) is reliable in the first assessment of these lesions, reserving other imaging techniques [e.g., computed tomography (CT) and magnetic resonance imaging (MRI)] for indeterminate US or when a complication is suspected. However, there is no evidence, from the literature, on the role of contrast-enhanced ultrasound (CEUS) in the evaluation of PVSA.

### Research frontiers

In recent years, CEUS has become progressively widespread in clinical practice, because of its several advantages in comparison to CT and MRI, such as the absence of nephrotoxicity and real-time evaluation. In view of these several advantages and the lack of evidence for PVSA, the aim of this study was to investigate the role of CEUS in the patients affected.

### Innovations and breakthroughs

In this study, CEUS was useful in the assessment and follow-up of a PVSA, by improving delineation of the lumen, its patency degree and integrity of the walls. CEUS was also useful to reveal a dynamic sign, the swirling pattern, that is equivalent to the "to-and-fro" sign found on color Doppler ultrasound and cannot be demonstrated on CT and MRI, because of their static modality of acquisition of images.

### Applications

The study found that CEUS is a reliable imaging modality in patients with PVSA. Future research is needed to confirm if CEUS could be used as an alternative method to CT and MRI, thus avoiding unnecessary CT radiation exposure and kidney damage in at-risk patients, after administration of iodine contrast or gadolinium.

### Terminology

CEUS is a safe imaging modality that allows real-time evaluation of intra-abdominal diseases, and consists of the acquisition of US images after intravenous administration of contrast agents which act as blood pool tracers and are constituted by gas surrounded by a membrane that prolongs their half-life and provides stability.

### Peer review

The paper is a very focused and thorough study of the proposed topics. I enjoyed reading it and I think it should be published after minimal corrections.

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