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Contrast-enhanced ultrasound of the liver: Vascular pathologies and interventions

Kontrastmittelunterstützte Sonografie der Leber: vaskuläre Pathologien und Interventionen

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Authors

Ehsan Safai Zadeh[1, 2], Helmut Prosch[1], Ahmed Ba-Ssalamah[1], Martina Scharitzer[1], Svitlana Pochepnia[1], Hajo Findeisen[3], Amjad Alhyari[2], Nils Raab[4], Katharina Paulina Huber[5], Christian Görg[2]

Affiliations

1 Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna, Vienna, Austria
2 Interdisciplinary Centre of Ultrasound Diagnostics, Gastroenterology, Endocrinology, Metabolism and Clinical Infectiology, University Hospital of Giessen and Marburg Campus Marburg, Marburg, Germany
3 Department for Internal Medicine, Red Cross Hospital Bremen, Bremen, Germany
4 Department for Internal Medicine, West Mecklenburg Hospital Helene von Bülow, Ludwigslust, Germany
5 Department of General Internal Medicine and Psychosomatics, University Hospital Heidelberg, Germany

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Correspondence

Ehsan Safai Zadeh
Department of Biomedical Imaging and Image-guided Therapy, Medical University of Vienna,
Währinger Gürtel 18–20, 1090 Vienna, Austria
ehsan.safaizadeh@meduniwien.ac.at

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ABSTRACT

Background Over the past two decades, contrast-enhanced ultrasound (CEUS) has been established as a method complementary to B-mode ultrasound and color Doppler sonography for diagnosing vascular liver pathologies and interventions.
Method The objective of this review is to elucidate the application of CEUS in diagnosing vascular pathologies and interventional procedures.
Results and Conclusion Considering the limitations of ultrasound, CEUS presents a similar alternative to other imaging modalities, such as computed tomography and magnetic resonance imaging, for evaluating vascular pathologies, guiding interventions, identifying complications, and assessing outcomes post intervention. Due to its widespread availability and the absence of radiation exposure, CEUS should be employed as a primary modality.

Key Points

- CEUS plays an important role in the detection of vascular liver pathologies.
- CEUS is helpful in characterizing vascular pathologies.
- CEUS is helpful in guiding interventions and identifying complications.

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ZUSAMMENFASSUNG

Hintergrund In den letzten zwei Jahrzehnten hat sich die kontrastmittelunterstützte Sonografie (CEUS) als ergänzende Methode zum B-Mode-Ultraschall und zur Farbdoppler-Sonografie bei der Diagnose vaskulärer Leberpathologien und Interventionen etabliert.

Methode Ziel dieser Übersicht ist es, die Anwendung der CEUS bei der Diagnose vaskulärer Pathologien und interventioneller Verfahren zu erläutern.

Ergebnisse und Schlussfolgerungen Unter Berücksichtigung der Limitationen des Ultraschalls stellt die CEUS eine vergleichbare Alternative zu anderen Bildgebungsverfahren wie der Computertomografie und der Magnetresonanztomografie dar, um vaskuläre Pathologien zu beurteilen und Interventionen zu leiten, Komplikationen zu identifizieren und die Ergebnisse nach der Intervention zu bewerten. Aufgrund der fehlenden Strahlenbelastung und der schnellen Verfügbarkeit sollte die CEUS als primäres Verfahren eingesetzt werden.

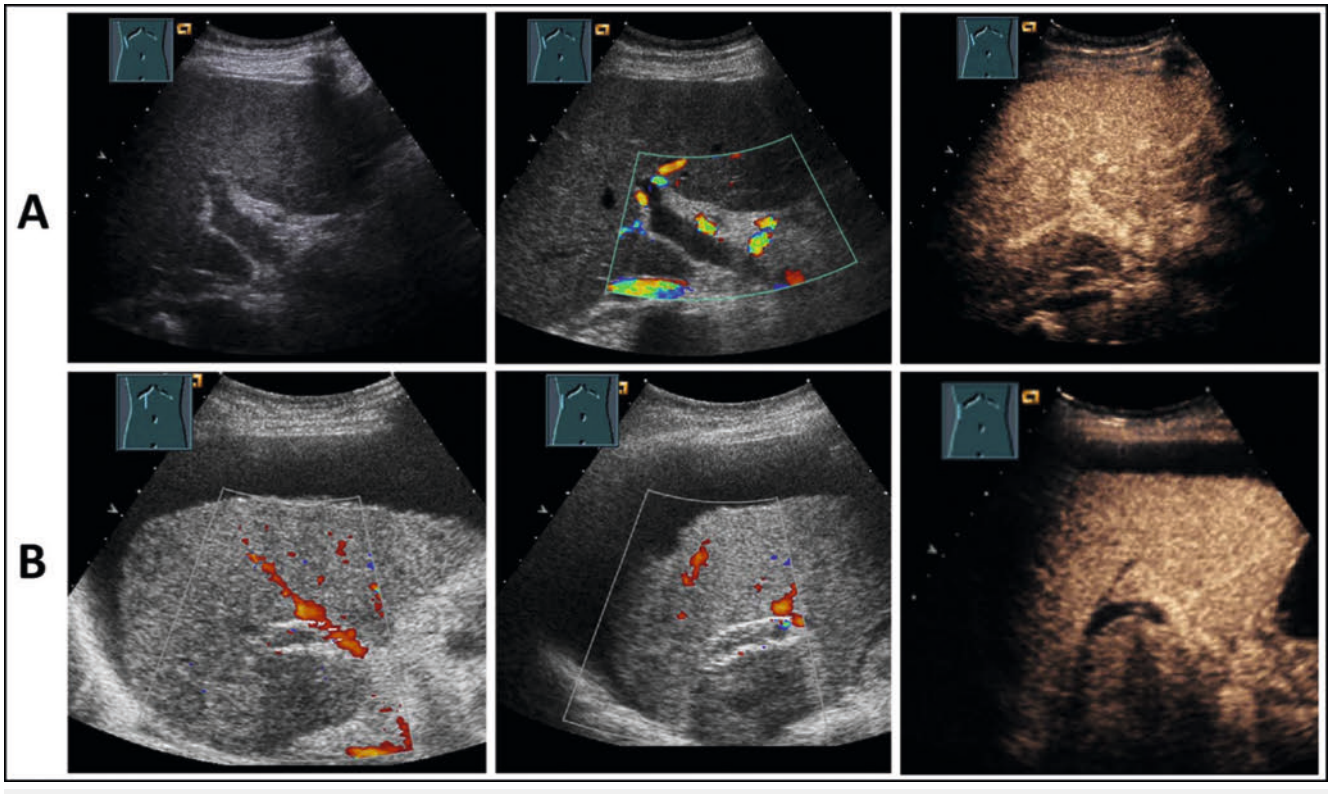
Kernaussagen

- Bei der Detektion vaskulärer Leberpathologien spielt die CEUS eine bedeutende Rolle.
- Die CEUS ist bei der Charakterisierung vaskulärer Pathologien hilfreich.
- Die CEUS ist hilfreich, um Interventionen zu leiten und Komplikationen zu identifizieren.

Introduction

Over the last two decades, contrast-enhanced ultrasound (CEUS) has established itself as a complementary, cost-effective, and radiation-free method of real-time diagnostics alongside B-image sonography (B-US) and color Doppler sonography (CDS) [1, 2, 3]. It is regularly used for relevant questions, especially in the field of liver pathologies. The basic principles for the application of CEUS have already been extensively described in several guidelines and reviews [1, 3, 4, 5].

The advantages of CEUS over the contrast media used in computed tomography (CT) include the lack of nephro- and thyroid toxicity and the strict intravascular dwell time [1, 2, 3]. The strict intravascular dwell time and the size of the microbubbles thus enable the visualization of perfusion at the capillary level [2]. Due to these advantages, taking into account the limitations of



▶ **Fig. 1** **A)** A 62-year-old patient with liver cirrhosis (Child B) of ethyl-toxic origin presenting with grade I esophageal varices according to the Paquet classification. Color Doppler ultrasonography shows no flow in the portal vein. Suspecting portal vein thrombosis, a contrast-enhanced ultrasound (CEUS) was performed. In this case, the portal vein in CEUS demonstrates enhancement, excluding thrombosis. **B)** A 66-year-old patient with liver cirrhosis (Child B) and post-transjugular intrahepatic portosystemic shunt (TIPS) for treatment-refractory ascites. Color Doppler ultrasonography reveals no flow signals. CEUS confirms the diagnosis of thrombotic occlusion.

ultrasound, CEUS represents an optimal method for assessing vascular liver pathologies [2, 3, 6] .

This review provides an overview of various vascular liver diseases and explains the role of CEUS in liver interventions.

Vascular Pathologies

Vascular pathology of the liver is suspected in the presence of a corresponding clinical condition and is rarely an incidental finding. CDS shows limited sensitivity in smaller vessels and in vessels with slow blood flow (less than 1 mm/s) [2] . CEUS can overcome these limitations by visualizing perfusion up to the capillary plane [2]. It can be used to exclude or confirm a questionable perfusion disorder in CDS (▶ **Fig. 1A** and **1B**).

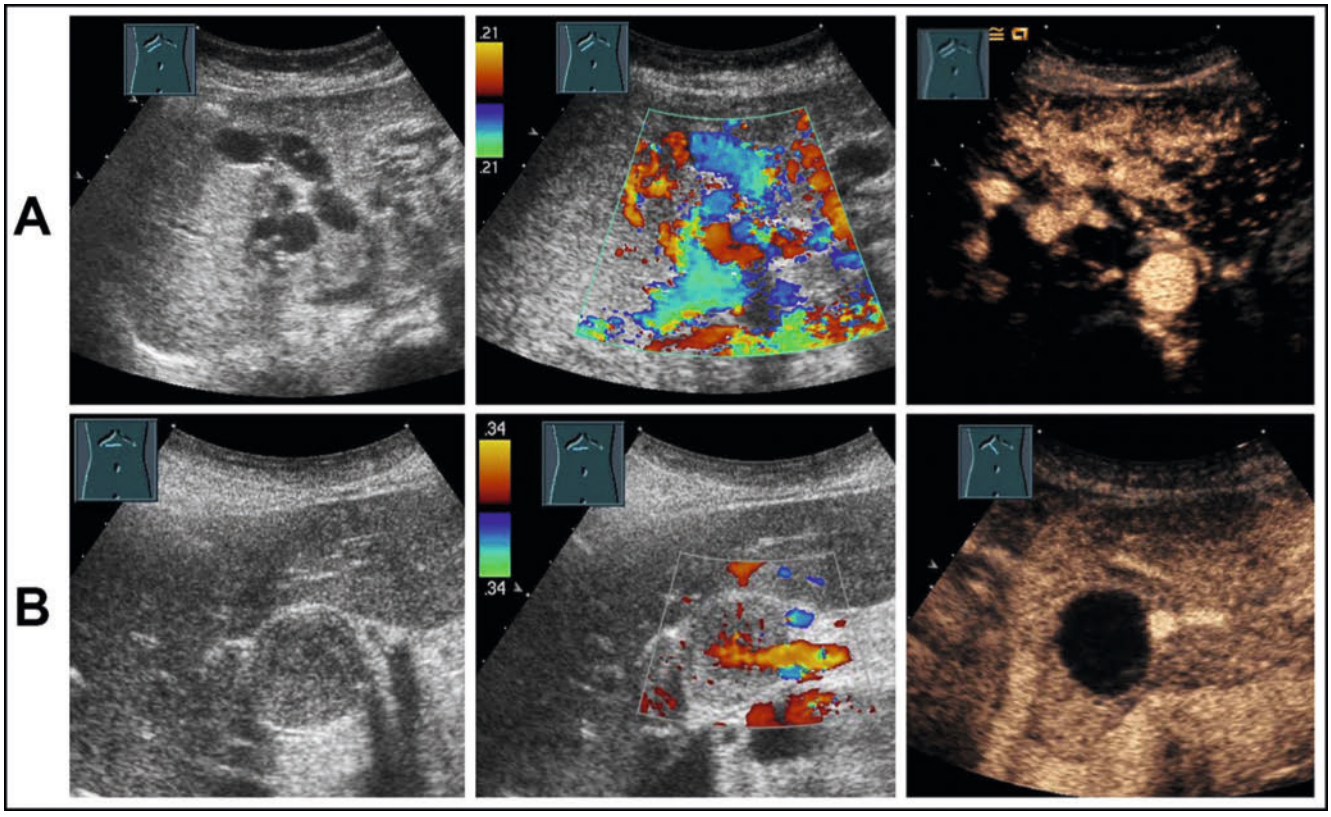
Arterial, Portal Venous and Venous Perfusion Disorder

The liver receives around 75 % to 80 % of its blood supply from the venous blood of the portal vein, while the remaining 20 % to 25 % is provided by the hepatic artery [7]. Vascular anomalies of the *hepatic artery,* such as in hereditary hemorrhagic telangiectasia (Osler's disease), hepatic aneurysm, or in the portal venous system, such as in spontaneous intrahepatic portosystemic shunt formations, are the domain of color Doppler ultrasonography. CEUS can provide additional information (▶ **Fig. 2**).

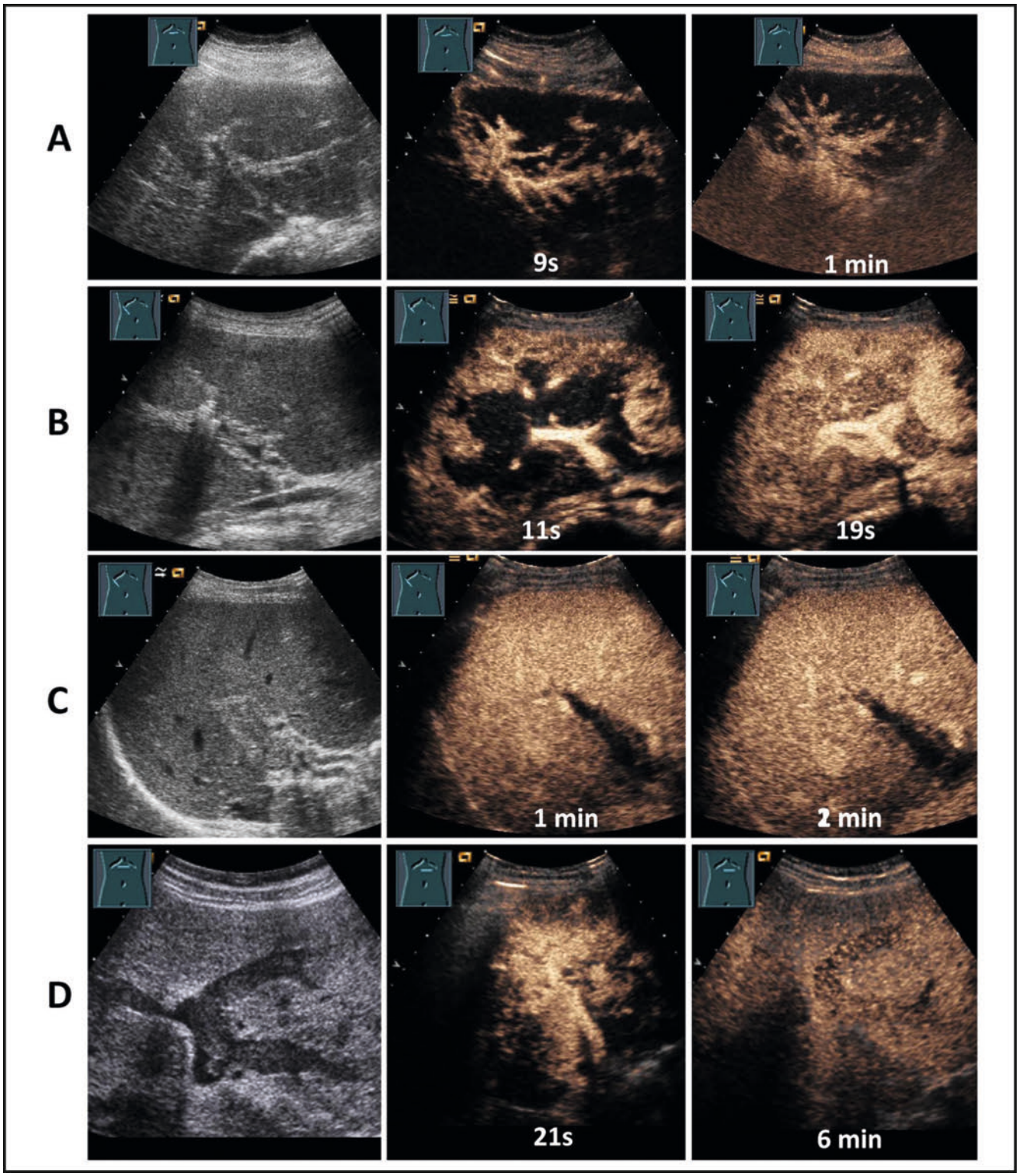
Due to this anatomical peculiarity of the liver, an occlusion of the hepatic artery does not necessarily lead to a liver infarction, as a sufficient oxygen supply is normally guaranteed by the portal vein [2, 7]. Liver infarctions are therefore rare and usually occur when there is a simultaneous portal vein obstruction. Liver infarctions have been described in cases of iatrogenic injury during interventions, such as cholecystectomy, transarterial chemoembolization, and transjugular intrahepatic portosystemic shunt placement, but also in systemic diseases, such as eosinophilic granulomatosis with polyangiitis, antiphospholipid syndrome, systemic lupus erythematosus, and liver abscesses [2, 8].

Portal vein thrombosis (PVT) occurs in patients with cirrhosis of the liver, myeloproliferative diseases, or coagulation disorders, such as factor V Leiden mutation, factor II-Mutation Antithrombin III deficiency, protein C or S deficiency [9]. It can also occur as part of a malignant disease, such as primary or secondary malignant liver tumors – for example hepatocellular carcinoma (HCC) or liver metastases [2, 9].

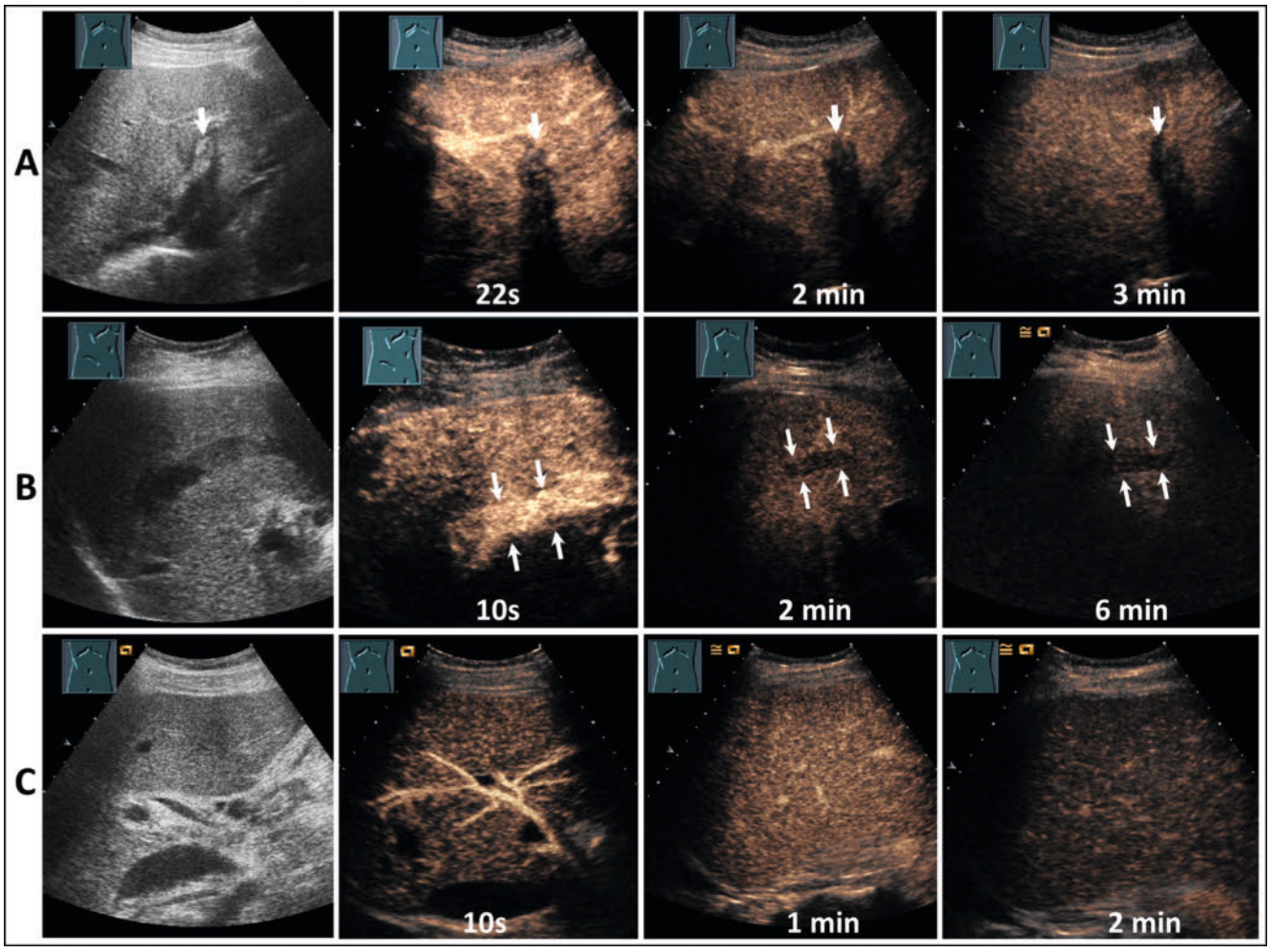
CEUS makes it possible to reliably distinguish between a dual perfusion disorder (hepatic infarction), a purely arterial, and a purely venous perfusion disorder. (▶ **Fig. 3A–C**). A lack of



▶ **Fig. 2** Illustration of possible vascular anomalies of the liver in contrast-enhanced ultrasound (CEUS). **A)** A 78-year-old patient with hereditary hemorrhagic telangiectasia and angiodysplasias in the stomach and cecum, condition after argon plasma coagulation; now presenting with anemia due to recurrent bleeding from the stomach; demonstration of liver involvement in B-mode ultrasound. The dilated vessels in the color Doppler ultrasonography and in the contrast-enhanced ultrasound show varicose arterial vessel volumes. **B)** A 94-year-old patient with acute biliary pancreatitis and an echogenic structure in the area of the liver hilum, adjacent to the hepatic artery. In the color Doppler ultrasonography, flow signals can be detected in the formation, as in a partially thrombosed aneurysm. However, in the CEUS, there is no perfusion throughout the examination, as in a completely thrombosed aneurysm.



▶ **Fig. 3** Demonstration of possible arterial and portal venous perfusion disorders of the liver in contrast-enhanced ultrasound (CEUS). **A)** A 34-year-old patient with HELLP syndrome and an inhomogeneous liver on B-mode ultrasound. In CEUS, the left lobe of the liver shows an absence of perfusion in both the arterial and portal venous phases, consistent with a liver infarction. **B)** A 44-year-old patient with colon cancer with a history of liver metastasis resection and arterial chemoembolization. B-mode ultrasound reveals a homogeneous liver. In CEUS, an area of absent perfusion is observed in the arterial phase, followed by present perfusion in the portal venous phase, consistent with an arterial perfusion disorder. **C)** A 22-year-old patient with hyperhomocysteinemia and echogenic material in the portal vein on B-mode ultrasound. In CEUS, the portal vein shows no perfusion throughout the examination, consistent with a bland thrombus. **D)** A 51-year-old patient with known hepatocellular carcinoma (HCC) and echogenic material in the portal vein on B-mode ultrasound. In CEUS, the echogenic material demonstrates contrast enhancement, consistent with a tumor thrombosis.

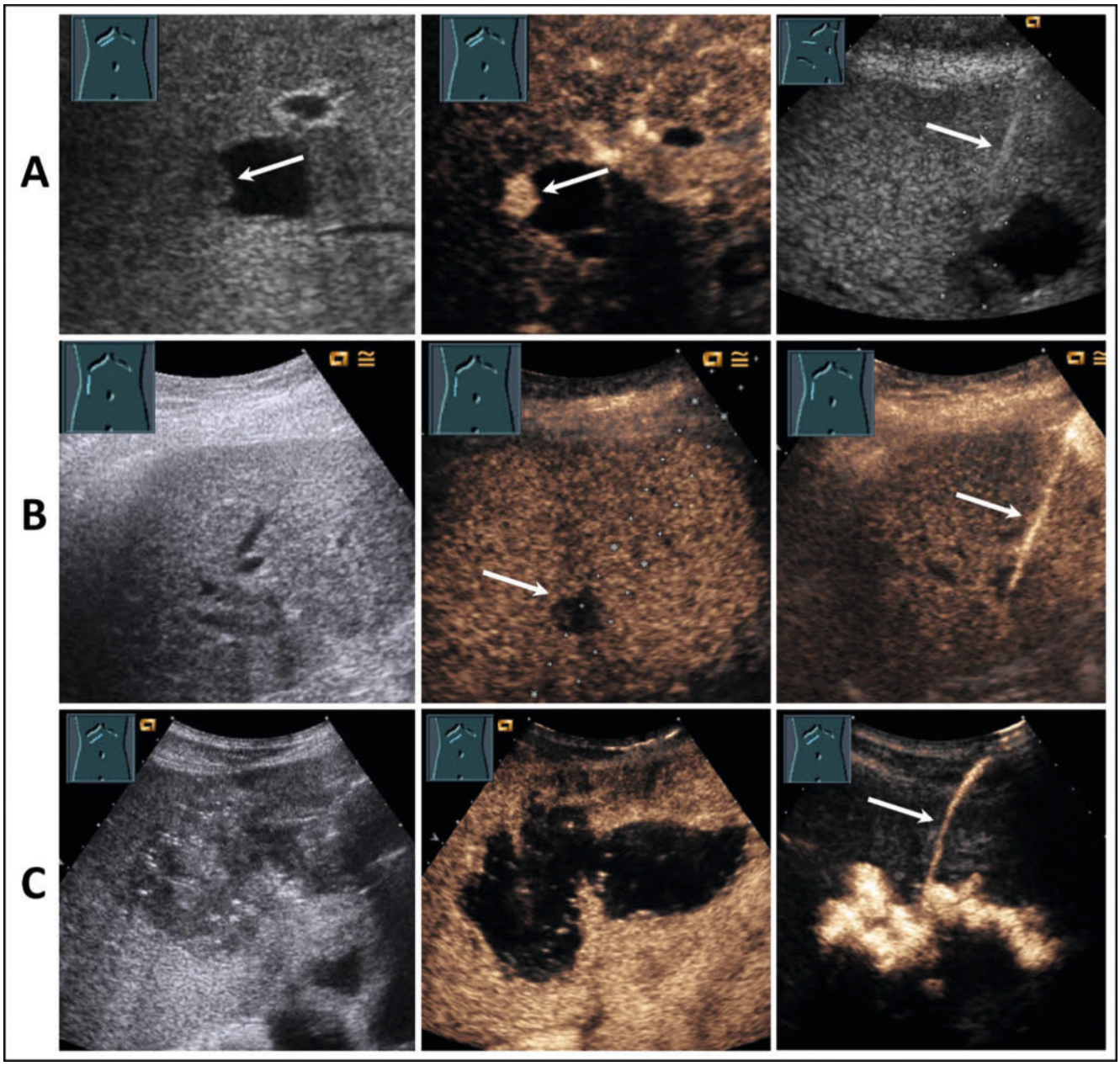


▶ **Fig. 4 A)** A 70-year-old patient with metastatic colorectal cancer and echogenic material in the left hepatic vein in B-mode ultrasound (arrow). In contrast-enhancement ultrasound (CEUS) (arrows), the vein shows no perfusion throughout the examination, consistent with a bland thrombus. **B)** A 63-year-old patient with primary undifferentiated hepatic sarcoma and echogenic material in the right hepatic vein in B-mode ultrasound. In CEUS, the echogenic material demonstrates contrast enhancement, consistent with a tumor thrombosis (arrows). **C)** A 20-year-old patient with acute myeloid leukemia and status post allogeneic stem cell transplantation, presenting with clinical signs of hepatic veno-occlusive disease. In B-mode ultrasound and the arterial phase, the hepatic hilum vessels are normal with regular enhancement after 1 minute and reduced enhancement after 2 minutes.

enhancement of the liver parenchyma during the entire examination indicates a dual perfusion disorder (liver infarction). Isolated lack of enhancement of the hepatic parenchyma during the arterial phase [10] (approx. 10–20 seconds after contrast media administration up to approx. 30–45 seconds) indicates an arterial perfusion disorder. Isolated lack of enhancement of the portal veins or their branches throughout the examination indicates a thrombus in the portal venous vascular system. In addition, CEUS is helpful in differentiating a tumor thrombus from a bland thrombus in the portal venous vascular system (▶ **Fig. 3C** and **3D**) [2, 11].

Obstruction of the large *outflowing hepatic veins* is referred to as Budd-Chiari syndrome (BCS) [2]. The obstruction can be partial or complete, and it can be primary or secondary. It leads to a secondary increase in sinusoidal pressure, portal hypertension, and a decrease in portal vein perfusion [2, 12]. Primary thromboses in the hepatic veins can be caused by thrombophilia, whereby clinical pictures such as factor V Leiden mutation, antithrombin III deficiency, protein C or S deficiency or acquired diseases, especially myeloproliferative disorders, are possible causes [2, 12]. Secondary Budd-Chiari syndrome can arise from compression of neighboring structures or from tumor invasion [12].

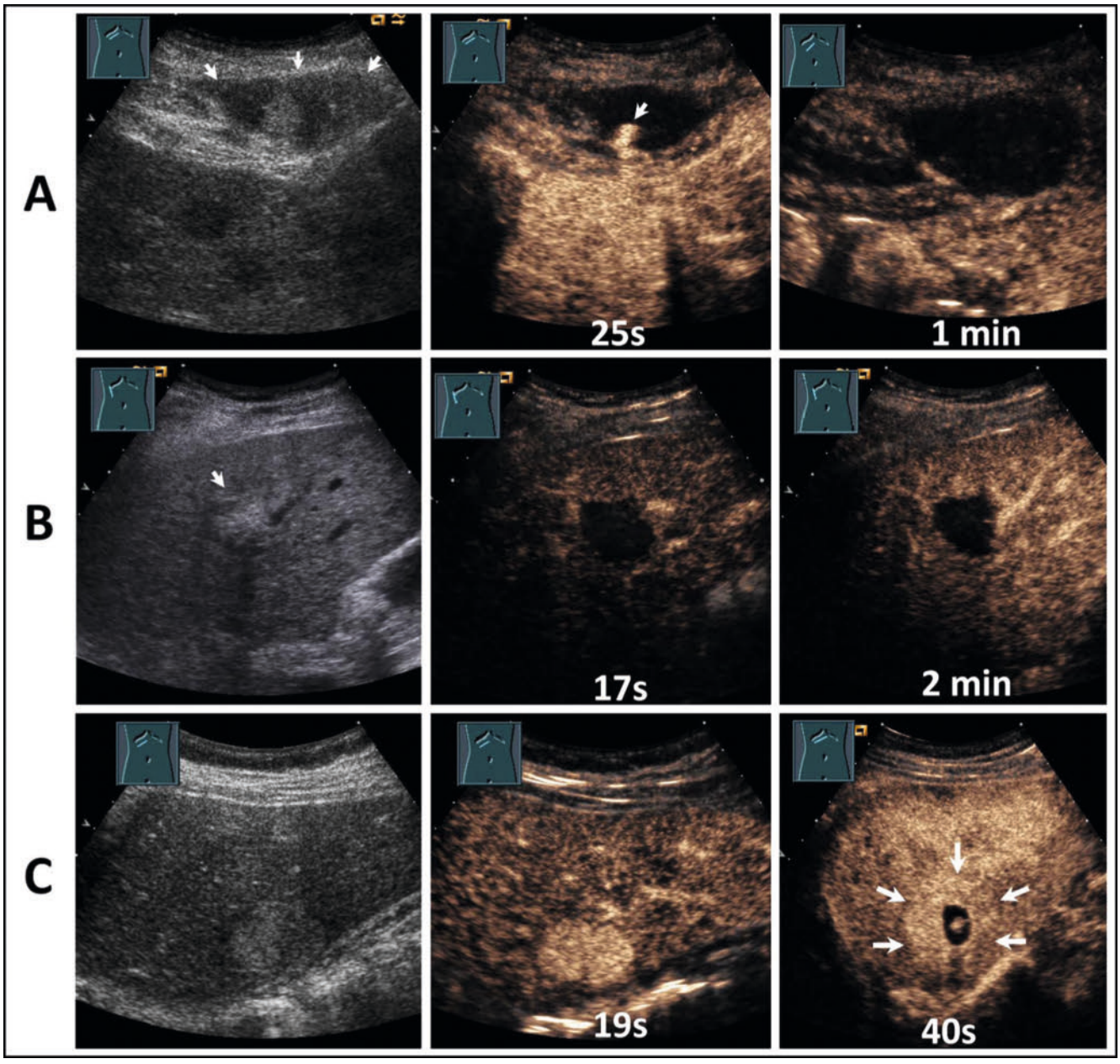
In complete or partial Budd-Chiari syndromes, thrombosis in the large hepatic veins can be differentiated as bland thrombus or tumor thrombosis with the help of CEUS (▶ **Fig. 4A** and **B**). Furthermore, initial case studies indicate that vein occlusion disease of the smallest hepatic veins (VOD) in the context of allogeneic bone marrow transplantation can result in a decrease in parenchymal enhancement [13] (▶ **Fig. 4C**).



▶ **Fig. 5 A)** A "Cyst-like" lesion in B-mode ultrasound with peripheral inhomogeneous demarcation (arrow). In contrast-enhancement ultrasound (CEUS), the peripheral area demonstrates hyperperfusion as seen in viable tissue (arrow), which was confirmed to be a metastasis of a known papillary renal cell carcinoma via ultrasound-guided biopsy (arrow). **B)** No liver lesion is discernible in a patient with pancreatic cancer in B-mode ultrasound, which becomes visible in CEUS (arrow). By biopsying the lesion in CEUS mode (arrow), a metastasis of the pancreatic cancer was confirmed. **C)** Presentation of a liver abscess in B-mode ultrasound and CEUS, with position control of the drainage catheter in CEUS mode after contrast agent application through the drainage (arrow).

CEUS-Guided Interventions for Focal Liver Space-Occupying Lesions

CEUS can be used to support diagnosis and better visualize the puncture target before intervention, for control during intervention, or to confirm the results after surgery [6]. It has been described that CEUS-guided biopsy increases the diagnostic accuracy of liver lesions by up to 10 % compared to non-CEUS-guided US biopsy [3, 14]. CEUS enables reliable differentiation between vital and avital tumor tissue due to the strictly intravascular interweaving and thus increases the success rate for punctures of liver foci (▶ **Fig. 5A**) [15]. Puncture in CEUS mode can still be used for focal lesions in the liver that cannot be clearly visualized in B-US (▶ **Fig. 5B**) [15, 16]. When inserting a catheter drainage into a liver abscess, CEUS with extravascular application of the contrast media via the drainage can be used to check the position of the catheter (▶ **Fig. 5C**) [17].



▶ **Fig. 6 A)** Patient after liver biopsy due to suspicion of liver metastases from breast cancer. The control 2 hours after the biopsy shows in B-mode ultrasound (left) an echogenic area above the biopsy location (arrows). In contrast-enhanced ultrasound (CEUS) (middle), a contrast agent extravasation (arrow) becomes visible, indicating active bleeding. After 4 hours, CEUS (right) shows the cessation of bleeding. **B)** Patient after radiofrequency ablation 6 months ago for hepatocellular carcinoma (HCC). During follow-up, the echogenic lesion (arrow) shows no enhancement throughout the examination, allowing the exclusion of a recurrence. **C)** Patient with HCC before transarterial chemoembolization (TACE) (middle) and after TACE (right), where the lesion shows incomplete enhancement as an indication of residual vital tumor tissue (arrows).

In the post-interventional procedure, CEUS can be used to detect/exclude post-interventional complications such as bleeding (▶ **Fig. 6A**), arteriovenous fistula, success monitoring of radiofrequency ablation (▶ **Fig. 6B**), or a transarterial chemoembolization (TACE) (▶ **Fig. 6C**) [6, 18].

Limitations

In contrast to CT and MR, CEUS is fundamentally characterized as an examination method that is highly dependent on the examiner. Therefore, the diagnostic value varies depending on the experience and competence of the examiner. In CEUS, similar to B-US, in patients with poor sonographic conditions, deeper areas may occasionally not be visualised due to substantial acoustic attenuation, and areas in the hepatic diaphragmatic dome may occasionally not be visualised due to overlying gas.

Conclusion

The implementation of CEUS in clinical practice has opened new horizons in the diagnosis of vascular liver pathologies and can support the diagnosis of a variety of vascular liver diseases [2]. Taking into account the primary use of ultrasound in liver diseases, CEUS, which can be performed quickly, without radiation exposure, and directly at the patient's bedside, enables rapid diagnosis and treatment [2, 6]. CEUS allows precise visualization of macro and micro vessels as well as the luminal integrity of the drainages in real time [6]. Advances in CEUS technology have made contrast-enhanced ultrasonography an indispensable tool in sonographic interventions, to guide the intervention, detect complications, and assess post-intervention results [6].

Conflict of Interest

C. Görg received funding from Bracco Imaging. Bracco Imaging supported CEUS workshops at the University Hospital Marburg.

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