ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

World J Gastroenterol 2024 October 7; 30(37): 4083-4167

Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

Contents

Weekly Volume 30 Number 37 October 7, 2024

ABOUT COVER

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG*, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now abstracted and indexed in Science Citation Index Expanded (SCIE), MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJG* as 4.3; Quartile: Q1. The *WJG*'s CiteScore for 2023 is 7.8.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Hua-Ge Yu*; **Production Department Director:** *Xu Guo*; **Cover Editor:** *Jia-Ru Fan.*

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORS-IN-CHIEF
Andrzej S Tarnawski

EXECUTIVE ASSOCIATE EDITORS-IN-CHIEF
Jian-Gao Fan (Chronic Liver Disease)

EDITORIAL BOARD MEMBERS
http://www.wjgnet.com/1007-9327/editorialboard.htm

PUBLICATION DATE
October 7, 2024

PUBLISHING PARTNER
Shanghai Pancreatic Cancer Institute and Pancreatic Cancer Institute, Fudan University
Biliary Tract Disease Institute, Fudan University

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

POLICY OF CO-AUTHORS
https://www.wjgnet.com/bpg/GerInfo/310

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

PUBLISHING PARTNER's OFFICIAL WEBSITE
https://www.shca.org.cn
https://www.zs-hospital.sh.cn

World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com

World J Gastroenterol 2024 October 7; 30(37): 4115-4131

DOI: 10.3748/wjg.v30.i37.4115

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

MINIREVIEWS

Pictorial review of hepatic echinococcosis: Ultrasound imaging and differential diagnosis

Yi Tao, Yi-Fei Wang, Jun Wang, Shuang Long, Barnabas C Seyler, Xiao-Fei Zhong, Qiang Lu

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification
Scientific Quality: Grade B, Grade C
Novelty: Grade B, Grade C
Creativity or Innovation: Grade B, Grade C
Scientific Significance: Grade A, Grade C

P-Reviewer: Fan Z; Kong X

Received: June 10, 2024
Revised: August 26, 2024
Accepted: September 12, 2024
Published online: October 7, 2024
Processing time: 107 Days and 21.6 Hours

Yi Tao, Yi-Fei Wang, Jun Wang, Xiao-Fei Zhong, Qiang Lu, Department of Medical Ultrasound, West China Hospital of Sichuan University, Chengdu 610041, Sichuan Province, China

Shuang Long, Department of Radiology, Gaoping District People's Hospital, Nanchong 637100, Sichuan Province, China

Barnabas C Seyler, Shude International, Chengdu Shude High School, Chengdu 610066, Sichuan Province, China

Barnabas C Seyler, Department of Environment, Sichuan University, Chengdu 610065, Sichuan Province, China

Corresponding author: Qiang Lu, MD, Professor, Department of Medical Ultrasound, West China Hospital of Sichuan University, No. 37 Guoxue Xiang, Chengdu 610041, Sichuan Province, China. luqiang@scu.edu.cn

Abstract

Echinococcosis is a zoonotic disease caused by parasites belonging to the genus *Echinococcus* that primarily affect the liver. The western plateau and pastoral areas of China are high-risk regions for hepatic cystic echinococcosis and hepatic alveolar echinococcosis (HAE). The high late mortality rate associated with HAE underscores the critical need for early diagnosis to improve cure rates and mitigate the disease burden in endemic areas. Currently, the World Health Organization recommends ultrasonography as the preferred initial screening method for hepatic echinococcosis. However, distinguishing between specific types of lesions, such as those of hepatic cystic echinococcosis and HAE, and other focal liver lesions is challenging. To address this issue, contrast-enhanced ultrasound is recommended as a tool to differentiate solid and cysto-solid hepatic echinococcosis from other focal liver lesions, significantly enhancing diagnostic accuracy. In this comprehensive review, we discuss the progression of hepatic echinococcosis and detail the imaging features of various types of echinococcosis using conventional, contrast-enhanced, and intraoperative ultrasound techniques. Our objective is to provide robust imaging evidence and guidance for early diagnosis, clinical decision making, and postoperative follow-up in regions with high disease prevalence.

Key Words: Echinococcosis; Zoonotic disease; Ultrasound; Contrast-enhanced ultrasound; Diagnosis

Core Tip: Accurate diagnosis of hepatic echinococcosis is crucial, especially for high-mortality hepatic alveolar echinococcosis. Ultrasonography is recommended as the first-line examination for hepatic echinococcosis in endemic areas. This review focuses on the clinical features and ultrasonographic diagnosis of this disease, emphasizing the importance of early detection in endemic regions to improve clinical outcomes. Additionally, this review presents classic images of conventional ultrasound, contrast-enhanced ultrasound, and intraoperative ultrasound to illustrate different stages and types of hepatic cystic and alveolar echinococcosis, thereby facilitating their differentiation from other focal liver lesions.

Citation: Tao Y, Wang YF, Wang J, Long S, Seyler BC, Zhong XF, Lu Q. Pictorial review of hepatic echinococcosis: Ultrasound imaging and differential diagnosis. *World J Gastroenterol* 2024; 30(37): 4115-4131
URL: https://www.wjgnet.com/1007-9327/full/v30/i37/4115.htm
DOI: https://dx.doi.org/10.3748/wjg.v30.i37.4115

INTRODUCTION

Echinococcosis is a parasitic disease caused by cestodes of the tapeworm genus *Echinococcus*. Depending on the pathogen, echinococcosis can be classified as alveolar echinococcosis (AE) caused by *Echinococcus multilocularis*, or cystic echinococcosis (CE) caused by *Echinococcus granulosus*[1,2]. The annual incidence of CE ranges from 1 to 200 per 100000 individuals, whereas the incidence of AE ranges from 0.03 and 1.2 per 100000 individuals[3].

The incidence of CE and AE in western China is among the highest globally, with AE accounting for 91% of new cases worldwide[4-8]. The endemic areas of echinococcosis in China cover 40% of the total land area, with at least 50 million people at risk of infection, especially herders and farmers. The average prevalence of hepatic echinococcosis is 0.51%, with some areas reporting rates of up to 14.3%[5,6,9-11]. Children are at high risk of echinococcosis. In the Qinghai-Tibet Plateau region of western China, the incidence of CE among school-aged children is 0.6%-0.8%, while the annual incidence of AE is 1.1%-1.3%[5,12,13]. From 2005 to 2020, the Chinese government implemented various control measures, including health education, in 370 endemic counties to achieve effective prevention and control[5,11,14-16]. Despite these efforts, implementing these methods in semi-nomadic communities has proven challenging[17].

Reports indicate that up to 98% of AE cases and 65%-80% of CE cases involve the liver[2,15,18,19]. The untreated mortality rate within 10-15 years of diagnosis for patients with hepatic CE (HCE) is 2%-4%, whereas that for patients with hepatic AE (HAE) is 90%-94%[2,15]. Therefore, early detection of hepatic echinococcosis is crucial to improve patient survival rates and reduce the disease burden[20]. Imaging examinations, including ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI), are accurate and useful in diagnosing hepatic echinococcosis [21,22]. Yet, the highly endemic regions of Western China are remote with limited resources, making access to MRI and CT scans challenging. The World Health Organization-Informal Working Group on Echinococcosis (WHO-IWGE) recommends the use of ultrasonography as the preferred method for screening hepatic echinococcosis in endemic areas, owing to its affordability, convenience, and accuracy. Furthermore, it is preferred for intraoperative localization and postoperative follow-up[2,23].

Nonetheless, ultrasound results are influenced by the experience level of radiologists. Furthermore, diagnostic capabilities differ between hospitals and regions. Therefore, in this study, we comprehensively reviewed and compared the pathogenesis, clinical features, and ultrasonic diagnosis of HAE and HCE, and presented classic images of hepatic echinococcosis using three ultrasound techniques [*i.e.*, conventional, contrast-enhanced, and intraoperative ultrasound (IOUS)]. Our aim is to improve the accuracy of the early diagnosis of hepatic echinococcosis in endemic areas.

THE PATHOPHYSIOLOGICAL MECHANISM AND CLINICAL MANIFESTATIONS OF HEPATIC ECHINOCOCCOSIS (HCE AND HAE)

Patients with echinococcosis may accidentally ingest adult parasite eggs released into the environment by definitive hosts (usually dogs) or intermediate hosts (*e.g.*, mice, cattle, and sheep)[5,15,24]. Upon entering the gastrointestinal tract, the eggs are stimulated by digestive fluids to develop into hexacanth larvae, which are then absorbed into the bloodstream through the intestinal wall. They subsequently disseminate into the liver through the portal venous system before entering the metacestode stage[2,20].

Patients with hepatic echinococcosis may remain asymptomatic for 5 to 15 years[3,25,26]. It is noteworthy that HAE exhibits infiltrative growth and may invade the hepatic portal system (40% of cases) and bile ducts. Common manifestations include obstructive jaundice and portal hypertension[23,27,28]. Furthermore, HAE can metastasize to other organs, such as the brain and lungs, through lymphatic and hematogenous routes[29]. In view of HAE resembling malignant tumors in its biological behavior, it is colloquially known as the "worm cancer".

Table 1 Comparison of clinical features between hepatic cystic echinococcosis and hepatic alveolar echinococcosis

	HCE	HAE
Endemic region	Worldwide	North America, northern and central Eurasia
Definitive host	Dogs and other canids	Red foxes and wolves
Intermediate host	Sheep, horses, cows and humans	Rats and humans
Type of growth	Concentric expansive growth	Vesicle-to-vesicle, infiltrative growth
Clinical symptoms	Epigastric discomfort and loss of appetite	Vague abdominal pain (upper right abdomen, 30%), jaundice (25%-30%), fatigue, weight loss, fever and chills
Imaging modalities	Ultrasound, CT, and MRI are used to evaluate the structures adjacent to the lesion, and FDG-PET is used to evaluate the activity of the lesion	
Immunological diagnosis	Relatively specific immune response to heat-resistant B antigen, with 20%-58% negative results	Sensitive, positive immune response to specific antigens such as Em2 or Em18, with 90% positive results
Treatment methods and prognosis	Surgical removal of active hydatid cyst to avoid extravasation of cystic fluid, supplemented with drug treatment, with a good prognosis	Radical resection, supplemented with drug therapy, with poor prognosis in the late stage
Postoperative imaging follow-up duration	> 3 years	> 10 years

HCE: Hepatic cystic echinococcosis; HAE: Hepatic alveolar echinococcosis; CT: Computed tomography; MRI: Magnetic resonance imaging; FDG-PET: Fluorodeoxyglucose-positron emission tomography.

The growth pattern of HCE manifests as an expansive growth. In approximately 70% of the cases, the cysts reach a diameter exceeding 10 cm or occupy more than 70% of the liver volume. The likelihood of gallbladder biliary fistula increases significantly, and reaches up to 79% when the cyst diameter exceeds 7.5 cm[2,21]. In cases of larger HCE cysts that rupture or become infected, severe complications, such as allergic reactions and septic shock, may occur[30] (Table 1).

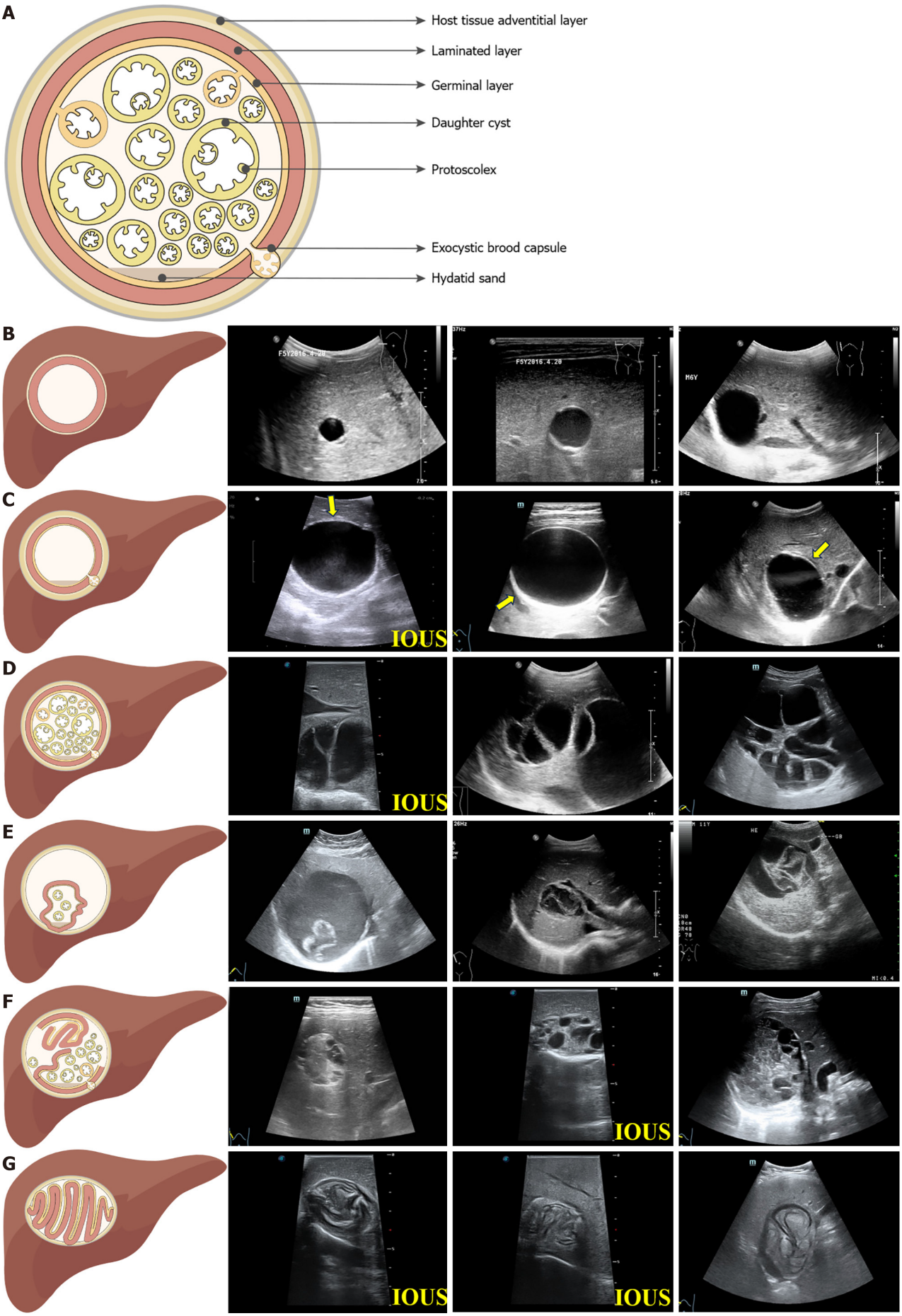
THE COURSE AND CLASSIFICATION OF HCE

The natural course of HCE can be divided into three stages: The early proliferative phase, the mid-stage of slow growth, and the late phase of growth arrest. Pathologically, HCE exhibits a distinct morphological structure comprising pericysts and hydatid. The pericyst is the adventitial layer of the host tissue that forms around the hydatid. The hydatid is composed of two layers, an outer laminated layer and an inner germinal layer, of which the latter is capable of forming protoscolex and daughter cysts (Figure 1A)[2,3]. The WHO-IWGE classifies CE into six types based on ultrasonographic imaging. These include cystic lesions (CL), CE1, CE2, CE3, CE4, and CE5[31].

GRAY-SCALE ULTRASONIC MANIFESTATIONS OF HCE

According to the classification criteria and expert consensus published by the associations, such as WHO-IWGE, Chinese Medical Association, and Chinese Medical Doctor Association[30-32], each CE type exhibits characteristic ultrasonic features, often with overlapping attributes. The first four types of CE are considered active and require therapeutic interventions. Conversely, CE4 and CE5 without symptoms or complications can be monitored regularly using ultrasonography. Accurate diagnosis and classification are crucial for guiding clinical treatment strategies. Understanding the characteristics of each CE subtype is helpful for early diagnosis. The primary manifestation of CL is a cystic occupation with an indistinct cyst wall (a fundamental sign) that is clearly visible on high-frequency ultrasonography (Figure 1B). In endemic regions, the discovery of cystic masses in the livers of children requires particular vigilance for differential diagnoses.

CE1 presents as a round, homogeneously echogenic, CL. Its key characteristics include the "double-wall sign" (a special sign) and the "snowflake sign" (a secondary sign). The "double-wall sign" manifests as a potential space between the inner and outer cyst walls, whereas the "snowflake sign" refers to dense, punctate echogenic deposits at the base of the cyst that float in the cystic fluid with changes in body position, also known as hydatid sand (Figure 1C). CE2 is primarily characterized by the "nested cysts/daughter cysts sign" (special signs). The cysts manifest as multiple daughter cysts within the mother. In addition, cysts may exhibit partitions resembling wheel-, petal-, or honeycomb-like structures (Figure 1D). CE3a is characterized by the detachment of the inner cyst and its subsequent floating in the cystic fluid, manifesting as the "water lily sign", "cuff sign", and "ribbon sign" (special signs) (Figure 1E). CE3b occurs when the inner cyst collapses after rupture, allowing cystic fluid to enter the space between the inner and outer cyst walls, resulting in a mixed echogenic mass with both solid and cystic components (Figure 1F). CE4 exhibits the characteristic "cerebral


A
Host tissue adventitial layer
Laminated layer
Germinal layer
Daughter cyst
Protoscolex
Exocystic brood capsule
Hydatid sand
B
C
D
E
F
G
IOUS
IOUS
IOUS
IOUS
IOUS

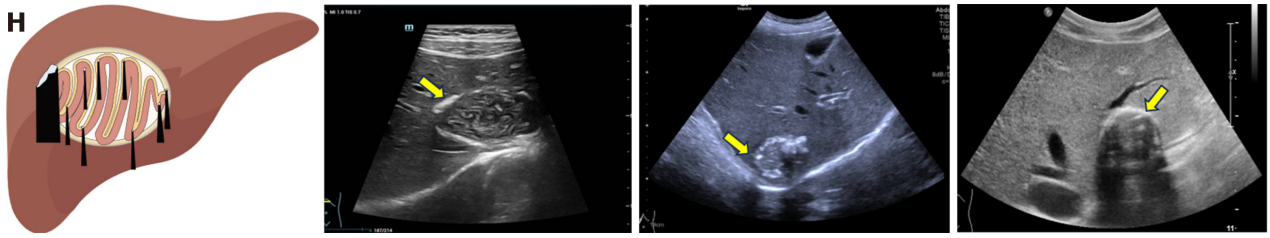


Figure 1 Schematic diagrams and grayscale ultrasound images of hepatic cystic echinococcosis. A: Schematic structure of hepatic cystic echinococcosis (HCE); B: Hepatic cystic lesions: Hepatic cystic lesions are characterized by indistinct cyst walls, which can be more effectively visualized using high-frequency ultrasound transducers; C: HCE1: HCE1 lesions manifest as spherical, homogeneously echogenic cystic masses, characterized by the presence of "double cyst wall" (the yellow arrow)and "snowflake" signs; D: HCE2: HCE2 lesions are characterized by "nested cysts" or "daughter cysts" and wheel-, petal-, or honeycomb-like appearances; E: HCE3a: Features of HCE3a lesions include the "water lily" sign and "ribbon" sign; F: HCE3b: HCE3b lesions manifest as cystic and solid masses with mixed echogenicity; G: HCE4: HCE4 lesions present alternating hypoechoic and hyperechoic masses, characterized by "ball of wool" and "cerebral gyri" signs; H: HCE5: HCE5 lesions refer to hyperechoic patches on the basis of the "cerebral gyrus" sign, with thickened and calcified cyst walls accompanied by a broad posterior acoustic shadow, referred to as the "eggshell calcified wall" sign (the yellow arrow). IOUS: Intraoperative ultrasound.

gyrus sign" and "ball of wool sign" (special signs), arising from the solidification of the degenerating cyst as the cystic fluid is absorbed and the cyst wall folds and contracts. The lesions appear as intermixed hypoechoic and hyperechoic masses (Figure 1G). CE5 presents with patchy hyperechoic regions on the basis of the "cerebral gyrus sign". The characteristic features include thickened and calcified cyst walls with a wide acoustic shadow behind them, collectively known as the "eggshell calcification wall sign" (a special sign) (Figure 1H).

The expert consensus recommends diagnostic criteria involving the detection of a liver mass in patients with a history of living in, or having contact with endemic areas[32]. A diagnosis can be made based on the presence of one or more special signs. Additionally, in cases where special signs are atypical, the presence of a secondary sign can be used as an auxiliary diagnostic tool to further strengthen the accuracy of the diagnosis (Table 2).

THE COURSE AND CLASSIFICATION OF HAE

Regarding the classification of HAE, a global consensus has yet to be reached. We attempted to categorize the disease according to the different stages of the disease's progression. Based on the evolution of HAE in terms of imaging, histopathology, and biological processes, three distinct stages can be identified, namely infiltrative, calcified, and liquefied[20,21,33-35]. During the infiltrative stage, HAE exhibits infiltrative growth through budding and continuously proliferates to produce new small vesicles that erode the surrounding tissue structures and form nodular lesions with boundaries indistinct from the normal liver parenchyma. As the disease enters the calcified stage, calcium salt deposition occurs because of infiltration and growth of the lesion, the inflammatory response of the body, and insufficient blood supply to the parasitic tissue. Early manifestations include punctate calcifications that later fuse into flocculent or large, irregular calcifications. Finally, during the liquefaction stage, when the HAE lesion proliferates into a large mass, the ischemic necrosis in the central region leads to the formation of irregular necrotic and liquefied cavities (Figure 2A).

Kern *et al*[33] proposed a standardized PNM classification system (P = parasitic mass in the liver, N = involvement of neighboring organs, and M = metastasis) for the clinical treatment of AE. Kodama *et al*[36] introduced an MRI-based classification method characterized by small vesicles, whereas Graeter and Schmidberger[35] presented a CT-based classification approach featuring the extent of calcification. These latter two methods reflect the biological evolution of AE to some extent[34,37]. In 2015, Kratzer *et al*[38] reported that the ultrasonographic manifestations of HAE could be categorized into six types: Hailstorm (54.1%), pseudocystic (13.5%), ossification (13.0%), hemangioma-like (8.1%), metastasis-like (6.5%), and unclassifiable (4.9%). Based on the disease progression, the infiltrative stage corresponds to the hemangioma-like and metastasis-like types, the calcified stage corresponds to the hailstorm and ossification types, and the liquefied stage corresponds to the pseudocystic type.

GRAY-SCALE ULTRASONIC MANIFESTATIONS OF HAE

According to the *Echinococcosis multilocularis* Ulm classification and the diagnostic consensus proposed by associations such as WHO-IWGE, Chinese Medical Association, and Chinese Medical Doctor Association[21,32,38], HAE exhibits characteristic ultrasonic manifestations across its three stages. On ultrasonography, infiltrative HAE presents as a solid mass with unclear boundaries, irregular morphology, and inhomogeneous echogenicity (a fundamental sign). This type is either hemangioma-like (Figure 2B) or metastasis-like. The metastasis-like type manifests as a hypoechoic mass without a halo ring, but with a small central hyperechoic, inhomogeneous scar (Figure 2C)[25,38].

The calcified HAE is predominantly represented by the hailstorm type, which is characterized by scattered, patchy, or irregular calcifications (a special sign) within heterogeneous echogenic masses with unclear boundaries and irregular morphology (Figure 2D). The ossification-type lesions exhibit clustered calcifications (a special sign) and a smaller lesion size than the hailstorm-type (Figure 2E). Liquefied HAE, described as the pseudocystic type, appears as a heterogeneous

Table 2 Sonographic features of hepatic cystic echinococcosis

WHO standardized classification	Disease course and prevalence	Sonographic features
CL	Uncertain, infertile cysts	Fundamental sign: Cystic occupations with indistinct cystic walls
Type CE1	Active, brood capsules; 21%-43%	Special sign: Double cyst wall. Secondary sign: Snowflake
Type CE2	Active, brood capsules; 4%-12%	Special signs: Nested cysts/daughter cysts (wheel-, petal-, or honeycomb-like)
Type CE3a	Transitional, the cysts begin to degenerate; 2%-8%	Special signs: Water lily, cuff sign, and ribbon
Type CE3b	Transitional, the cysts begin to degenerate; 2%-8%	Cystic and solid mass with mixed echogenicity
Type CE4	Inactive, most do not contain viable protoscolex; 10%-27%	Special signs: Ball of wool and cerebral gyri
Type CE5	Inactive, most do not contain viable protoscolex; 1%-11%	Special sign: Eggshell calcified wall

WHO: World Health Organization; CL: Cystic lesions; CE: Cystic echinococcosis.

Table 3 Sonographic features of hepatic alveolar echinococcosis

Course of disease	EMUC-US	Sonographic features
Infiltration stage	Hemangioma-like/metastasis-like	Fundamental sign: A solid, heterogeneously echoic mass with unclear boundaries and an irregular shape
Calcification stage	Hailstorm/ossified	Special sign: A heterogeneously echoic mass with punctate, gravel-like, and small circular echogenic calcifications inside, accompanied by a posterior acoustic shadow
Liquefaction stage	Pseudocystic	Special sign: A heterogeneously echoic mass with large, irregularly shaped dark areas, creating a "lava-like" appearance, referred to as the "cavity" sign

EMUC-US: *Echinococcosis multilocularis* Ulm classification-ultrasound.

mass with an irregular and inhomogeneous hyperechoic rim thicker than 10 mm. The interior of the mass is a hypoechoic area of liquefied necrosis with posterior acoustic enhancement, presenting with a "worm-eaten" or "lava-like" appearance, also known as the "cavity sign" (a special sign) (Figure 2F). The expert consensus recommends that the diagnostic criteria for HAE include the presence of basic lesions combined with one of the special signs[32] (Table 3).

CONTRAST-ENHANCED ULTRASONIC MANIFESTATIONS OF HEPATIC ECHINOCOCCOSIS

Mastering the characteristics of conventional ultrasound imaging can assist in the diagnosis. For instance, the most common hailstorm-type HAE appears as a solid mass accompanied by diffuse calcifications and lacks blood flow signals [20,38]. This distinguishes it from the most common malignant tumor, hepatocellular carcinoma (HCC), which typically lacks significant internal calcification but exhibits abundant blood flow. Conventional ultrasound still has certain limitations, such as the inability to reliably distinguish between metastasis-like HAE lesions and liver metastases, as well as between hemangioma-like HAE lesions and typical hemangiomas[25,26].

Contrast-enhanced ultrasound (CEUS) is of great value for the early diagnosis of HAE, with an accuracy rate significantly higher than that of conventional ultrasound (approximately 91%)[25,26,39-41]. CEUS can effectively evaluate the microvascular supply and blood perfusion in the infiltrating and proliferative regions of HAE, demonstrating comparable performance to CT and MRI in delineating lesion boundaries[23,29].

On CEUS, the primary feature of HCE is the absence of visible internal enhancement, with or without peripheral enhancement (Figure 3). The typical enhancement pattern of HAE on CEUS manifests as a "rim-like" or "worm-eaten" enhancement zone around the periphery of the lesion from the early arterial phase (AP) to the late portal venous phase (PVP), whereas the interior of the lesion remains unenhanced, forming a characteristic "black hole sign" (Figure 4)[25,26,39,42]. The interior of an HAE lesion is usually composed of clustered vesicles, calcifications, and necrotic areas, resulting in the absence of enhancement. Heterogeneous internal enhancement, if present, may be associated with residual liver tissue and lesion size[42-44]. Partially blurred enhancement at the edges of the HAE lesions was mainly due to the surrounding fibrosis and granulomatous reactions. Annular enhancement at the edge of the HAE lesion is primarily due to the presence of a marginal zone with abundant microvascular supply between the lesion and surrounding normal liver parenchyma[20,29,45,46]. Microscopic examination with CD34 immunostaining demonstrated an abundant accumulation

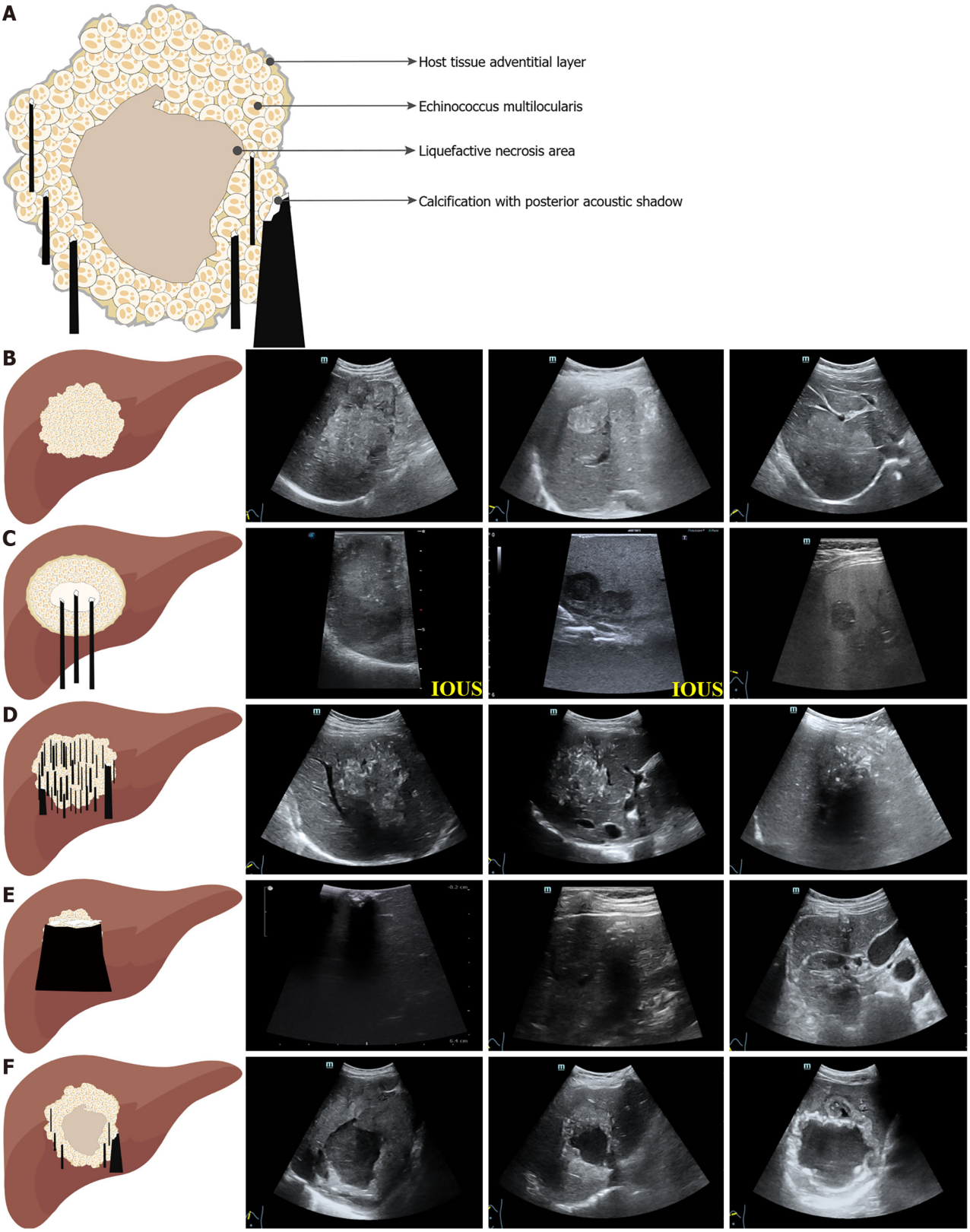


Figure 2 Schematic diagrams and grayscale ultrasound images of hepatic alveolar echinococcosis. A: Schematic structure of hepatic alveolar echinococcosis (HAE); B: Hemangioma-like: Hemangioma-like lesions of HAE manifest as well-defined and heterogeneous hyperechoic masses in comparison to the surrounding hepatic parenchyma; C: Metastasis-like: Metastasis-like lesions of HAE manifest as hypoechoic masses with indistinct margins, lacking a halo sign, and with a hyperechoic and heterogeneous scar at their center; D: Hailstorm: Hailstorm lesions of HAE are characterized by ill-defined boundaries and irregularly shaped masses of heterogeneous echogenicity, accompanied by scattered or diffuse calcifications, with or without a posterior acoustic shadow; E: Ossification: Ossified lesions of HAE present as small and sharply delineated lesions with internal clumps of calcification and a posterior acoustic shadow; F: Pseudocystic: Pseudocystic lesions of HAE are primarily characterized by a thickness exceeding 10 mm with high echogenicity, irregular and non-uniform margins, and a low-echogenicity liquefied necrotic area inside. IOUS: Intraoperative ultrasound.

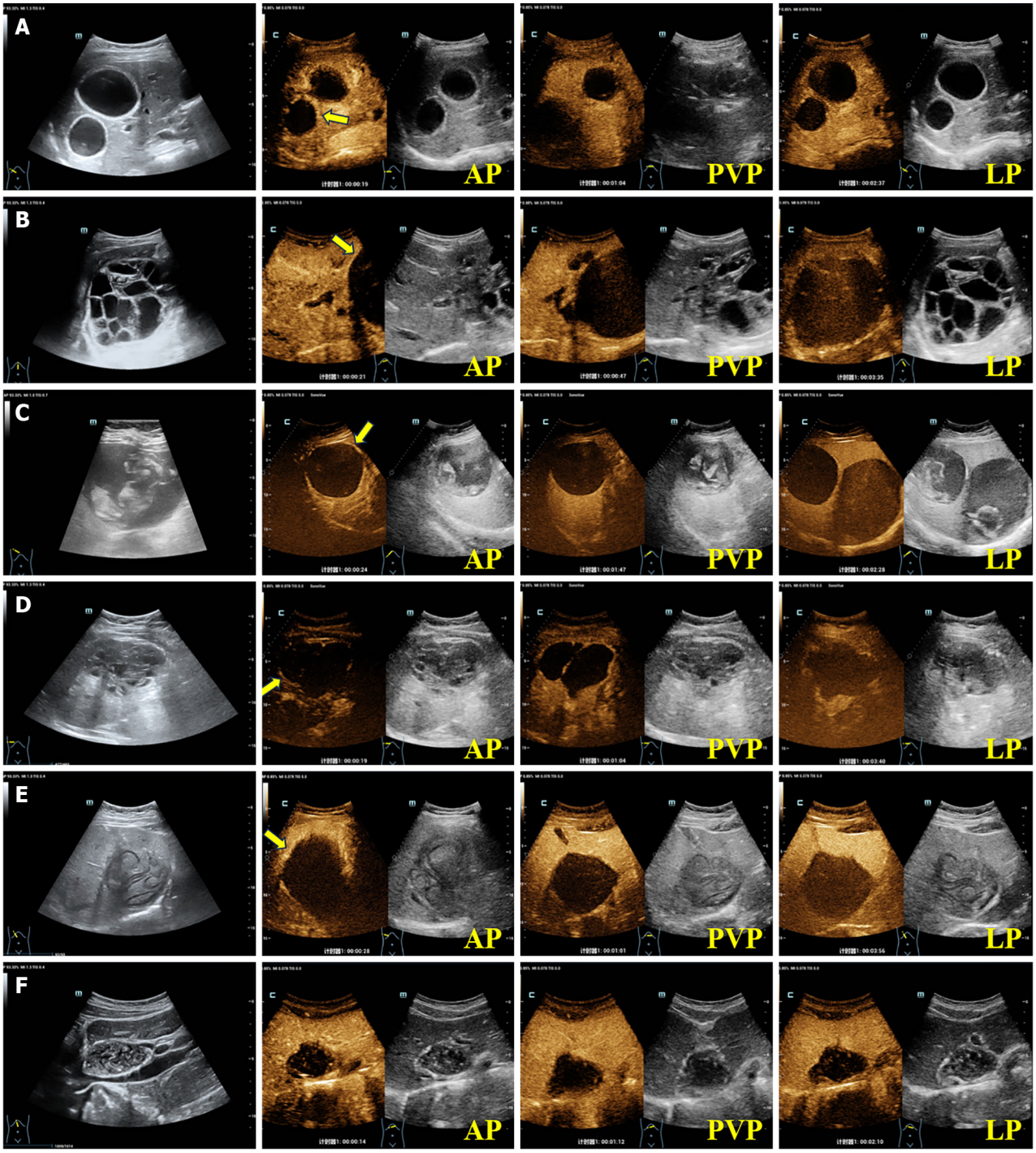


Figure 3 Contrast-enhanced ultrasound images of hepatic cystic echinococcosis. A: A 27-year-old female patient presenting with a liver lesion of hepatic cystic echinococcosis 1 (HCE1), exhibiting peripheral "rim-like" enhancement in the arterial phase (AP) on contrast-enhanced ultrasound (CEUS) (the yellow arrow), with no internal enhancement observed; B: A 41-year-old female patient presenting with a liver lesion of HCE2, exhibiting slightly peripheral "rim-like" enhancement in the AP on CEUS (the yellow arrow), with no internal enhancement detected; C: A 56-year-old female patient presenting with a liver lesion of HCE3a, exhibiting slightly peripheral "rim-like" enhancement in the AP on CEUS (the yellow arrow), with no internal enhancement observed; D: A 49-year-old male patient presenting with a liver lesion of HCE3b, exhibiting slightly peripheral "rim-like" enhancement in the AP on CEUS (the yellow arrow), with internal septal enhancement visible; E: A 47-year-old female patient presenting with a liver lesion of HCE4, exhibiting slightly peripheral "rim-like" enhancement in the AP on CEUS (the yellow arrow), with no internal enhancement observed; F: A 29-year-old female patient presenting with a liver lesion of HCE5, with no obvious enhancement in the AP, portal venous phase, or late phase.

of deeply stained red-brown cells in the peripheral zones of 92.5% of HAE lesions, confirming the formation of numerous neovascularizations within the marginal zone and indicating that the HAE lesions were in a relatively active stage[45,47]. The marginal zone is closely related to the lesion activity; therefore, it may be helpful for radical resection, which is crucial for preventing recurrence.

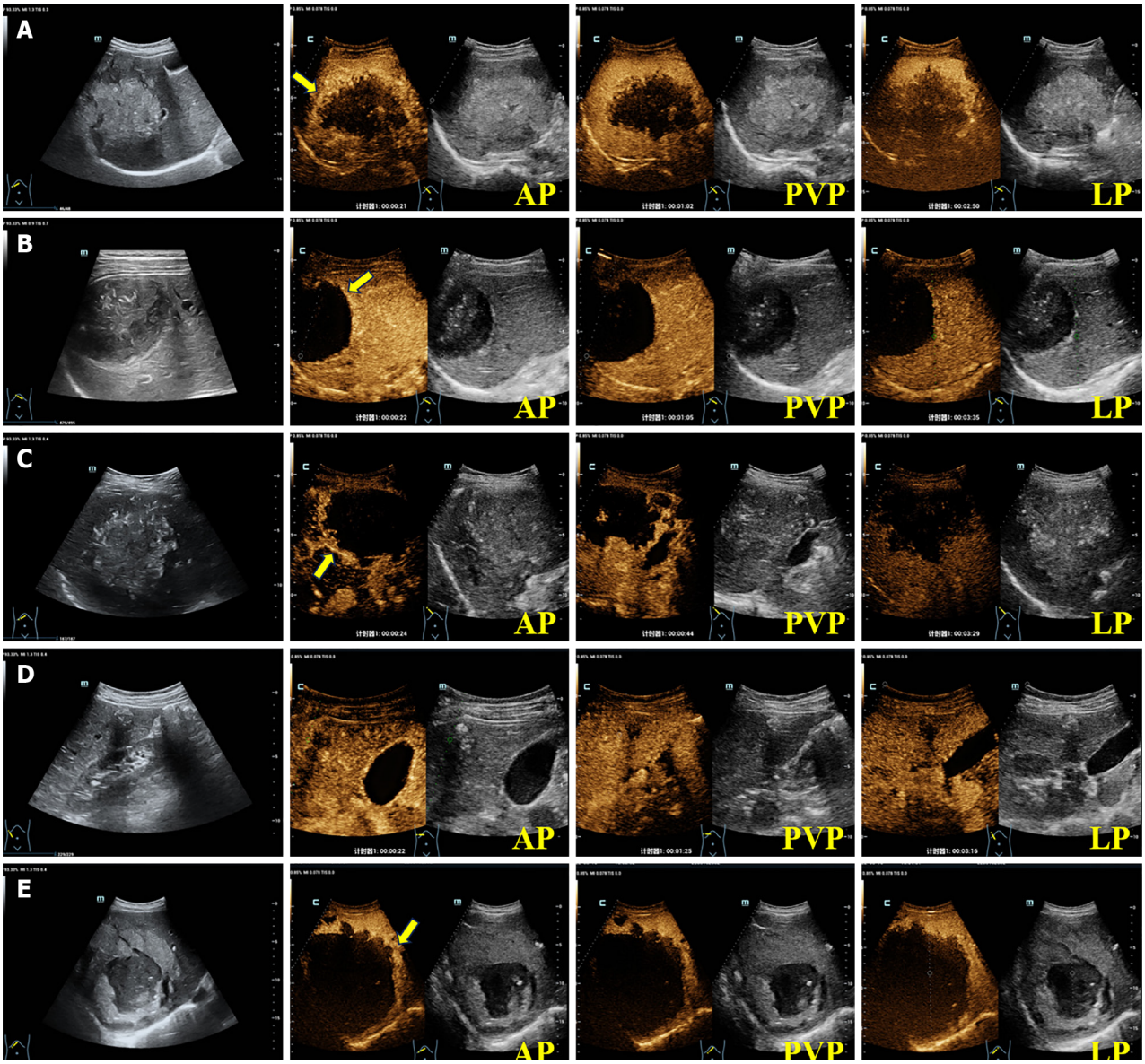


Figure 4 Contrast-enhanced ultrasound images of hepatic alveolar echinococcosis. A: A 55-year-old male patient presenting with a hemangioma-like hepatic alveolar echinococcosis (HAE) liver lesion, exhibiting peripheral "rim-like" enhancement in the arterial phase (AP) on contrast-enhanced ultrasound (CEUS) (the yellow arrow), with no internal enhancement; B: A 29-year-old female patient presenting with a metastasis-like HAE liver lesion, exhibiting peripheral "rim-like" enhancement in the AP on CEUS (the yellow arrow), with no internal enhancement; C: A 53-year-old female patient presenting with a hailstorm HAE liver lesion, exhibiting peripheral "rim-like" enhancement in the AP on CEUS (the yellow arrow), with no internal enhancement; D: A 50-year-old male patient presenting with an ossified HAE liver lesion, with no obvious enhancement in the AP, portal venous phase, or late phase; E: A 40-year-old female patient presenting with a pseudocystic HAE liver lesion, exhibiting peripheral "rim-like" enhancement in the AP on CEUS (the yellow arrow), but lacking internal enhancement.

DIFFERENTIAL DIAGNOSIS OF SOLID HEPATIC ECHINOCOCCOSIS VERSUS OTHER FOCAL LIVER LESIONS

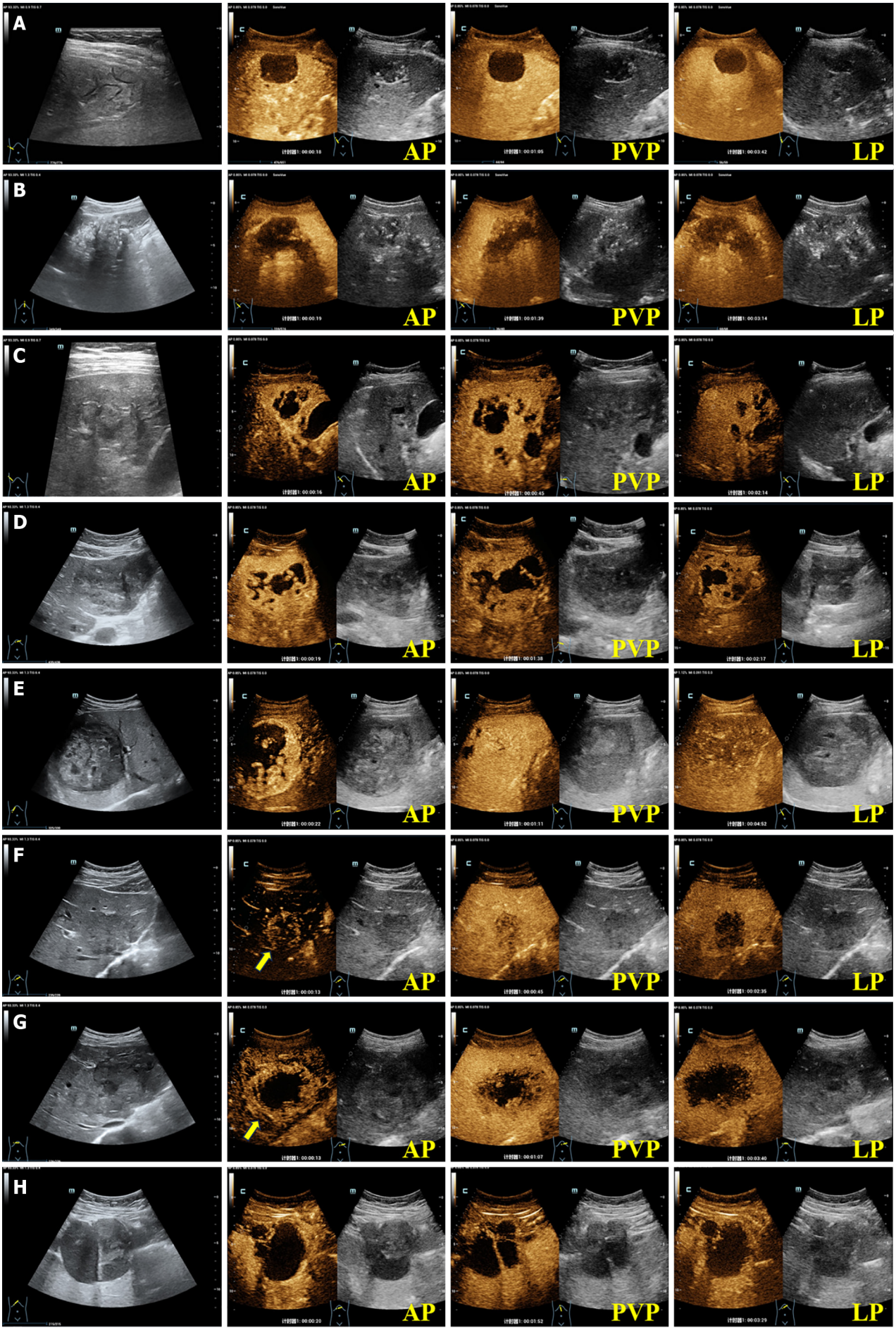
Certain solid and cysto-solid lesions of hepatic echinococcosis often present with ultrasonic features that overlap with those of focal liver lesions (FLLs), making their differentiation challenging, particularly for HAE lesions[32,43,48]. However, CEUS is a valuable tool for the differential diagnosis[25,26,39,49,50] (Table 4): (1) Hepatic paragonimiasis typically manifests as irregularly shaped, heterogeneously echoic areas with inhomogeneous enhancement on CEUS, associated with the presence of "sieve-like" and tunnel-shaped non-enhancing regions. The enhancement pattern of "fast in and slow out" of hepatic paragonimiasis has been reported (Figure 5C)[51]; (2) Mature liver abscesses commonly present as cystic masses with thick walls and septa. Sometimes, gas-fluid levels were observed within the cysts. In the AP, both the cyst wall and internal septations demonstrate enhancement, and multiple non-enhancing liquefied necrotic areas are visible within the cyst, presenting as a "honeycomb sign" (Figure 5D)[52]. Mature liver abscesses must be distinguished from pseudocystic HAE; (3) HCC is the most common primary malignant tumor of the liver and often occurs in patients with high-risk factors such as chronic hepatitis B or cirrhosis. Typically, these tumors exhibit expansive growth patterns. On CEUS, typical HCC lesions demonstrate inhomogeneous hyperenhancement in the AP, with a later washout

Table 4 Differential diagnosis of solid hepatic echinococcosis

Entities	Medical history	Sonographic features	Laboratory examination
HCE (HCE4, HCE5)	History of travel to endemic areas	B-mode: The mass shows the "cerebral gyri" sign with intermittent hyperechoic and hypoechoic signals, as well as scattered, annular, and "eggshell-like" calcification. CEUS: Most of the masses show no enhancement in both their interior and margins	Heat-resistant B antigen, with 20%-58% negative results
HAE	History of travel to endemic areas	B-mode: An ill-defined, heterogeneously echoic mass with diffuse, scattered, or focal calcification and possible liquefactive necrosis. CEUS: In the AP, an enhanced and irregular "rim-like" peripheral band can be observed surrounding the lesion, with no obvious internal enhancement, presenting as a "black hole" sign	Specific antigens such as Em2 or Em18, with 90% positive results
Hepatic paragonimiasis	History of eating undercooked shrimp and crabs	B-mode: An irregularly shaped and heterogeneous lesion with an internal appearance resembling "tunnel-like" echoes. CEUS: The lesion shows uneven enhancement in the AP, with non-enhancing reticular and "tunnel-like" areas internally	Stool examination
Liver abscess	History of diabetes, high fever, pain upon percussion in the liver area	B-mode: Thick-walled septated cystic lesions with areas of liquefied necrosis, including some with an air-fluid level within the cysts. CEUS: The mature liver abscess shows hyper-enhancement of the cystic wall and internal septa in the AP, with multiple patches of non-enhancing liquefied necrotic areas, resembling a "honeycomb-like" pattern	CBC, CRP
HCC	History of underlying liver disease associated with hepatitis and alcohol intake	B-mode: Swelling growth with a "hump" sign. CEUS: The typical HCC shows uniform hyper-enhancement in the AP and begins to wash out with slightly lower enhancement in the LP	AFP, AT
ICC	History of hepatolithiasis	B-mode: An ill-defined lesion, often accompanied by biliary duct dilation and early metastasis to hepatic hilar lymph nodes. CEUS: The mass-forming ICC shows irregular "rim-like" peripheral enhancement in the AP, washout in the PVP, and significant hypo-enhancement in the LP	CA 19-9
Liver metastases	Mainly arising from primary cancers of the lung, gastrointestinal tract, pancreas, and breast	B-mode: Multiple hypoechoic or hyperechoic masses within the liver. CEUS: The mass shows a thick "rim-like" hyper-enhancement in the early AP, washout in the late AP, and significant hypo-enhancement in the PVP and LP, presenting as a "bull's eye" sign	CEA, CA 72-4, CA 15-3, CA 125, CA 19-9
HBCA	Mainly in middle-aged women	B-mode: The cystic-solid mass with mixed echogenicity has a "multi-room-like" structure, often with solid wall nodules growing towards the cavity. CEUS: The enhancement of the lesion can be observed in "multilocular-like" septa, walls, and wall nodules in the AP	-
HCA	Women who take oral contraceptives	B-mode: A well-defined, homogeneous mass with clear borders. CEUS: The mass shows overall high enhancement in the AP and primarily iso-enhancement in the PVP and LP	-
FNH	Mainly in young and middle-aged women	B-mode: Central scar with a radial distribution within the mass. CEUS: The typical FNH presents as centrifugal enhancement in a "spoke-wheel" or "firework-like" pattern from the center to the periphery in the AP, with slight hyper-enhancement in the PVP and LP	-
HSH	-	B-mode: A "sieve pore-like" hyperechoic mass. CEUS: The typical HSH shows discontinuous, nodular peripheral enhancement in the AP, with progressive partial or complete centripetal fill-in in the PVP and slight hyper-enhancement in the LP. A non-enhancing area can be observed within the lesion	-
Hepatoblastoma	Predominantly in children under five years of age	B-mode: A slightly lobulated, heterogeneously echogenic mass with visible liquefied necrotic areas. CEUS: The mass shows hyper-enhancement in the AP and begins to wash out in the PVP, with no enhancement in the liquefied necrotic zone	AFP

HCE: Hepatic cystic echinococcosis; CEUS: Contrast-enhanced ultrasound; HAE: Hepatic alveolar echinococcosis; AP: Arterial phase; CBC: Complete blood cell count; CRP: C-reactive protein; HCC: Hepatocellular carcinoma; LP: Late phase; AFP: Alpha fetoprotein; AT: Abnormal thrombin; ICC: Intrahepatic cholangiocarcinoma; PVP: Portal venous phase; CA: Carbohydrate antigen; CEA: Carcinoembryonic antigen; HBCA: Hepatic biliary cystadenoma; HCA: Hepatocellular adenoma; FNH: Focal nodular hyperplasia; HSH: Hepatic sclerosing hemangioma.

time than other primary liver malignancies. Only mild regression was observed during the parenchymal phase (Figure 5E)[49,50,53-55]; (4) Intrahepatic cholangiocarcinoma (ICC) is the second most common primary malignant tumor of the liver and is categorized into mass-forming, periductal-infiltrating, and intraductal-growth types. The CEUS appearance of the mass-forming type ICC typically exhibits irregular "rim-like" enhancement in the AP, followed by early washout in the PVP and significant hypo-enhancement in the late phase (LP) (Figure 5F). This malignancy is often accompanied by lymph node metastasis in the hepatic portal region. Both HAE and ICC can lead to contraction of adjacent liver tissue and dilation of bile ducts, but they exhibit different patterns on CEUS[39,50,54]; (5) Liver metastases


A
AP
PVP
LP
B
AP
PVP
LP
C
AP
PVP
LP
D
AP
PVP
LP
E
AP
PVP
LP
F
AP
PVP
LP
G
AP
PVP
LP
H
AP
PVP
LP

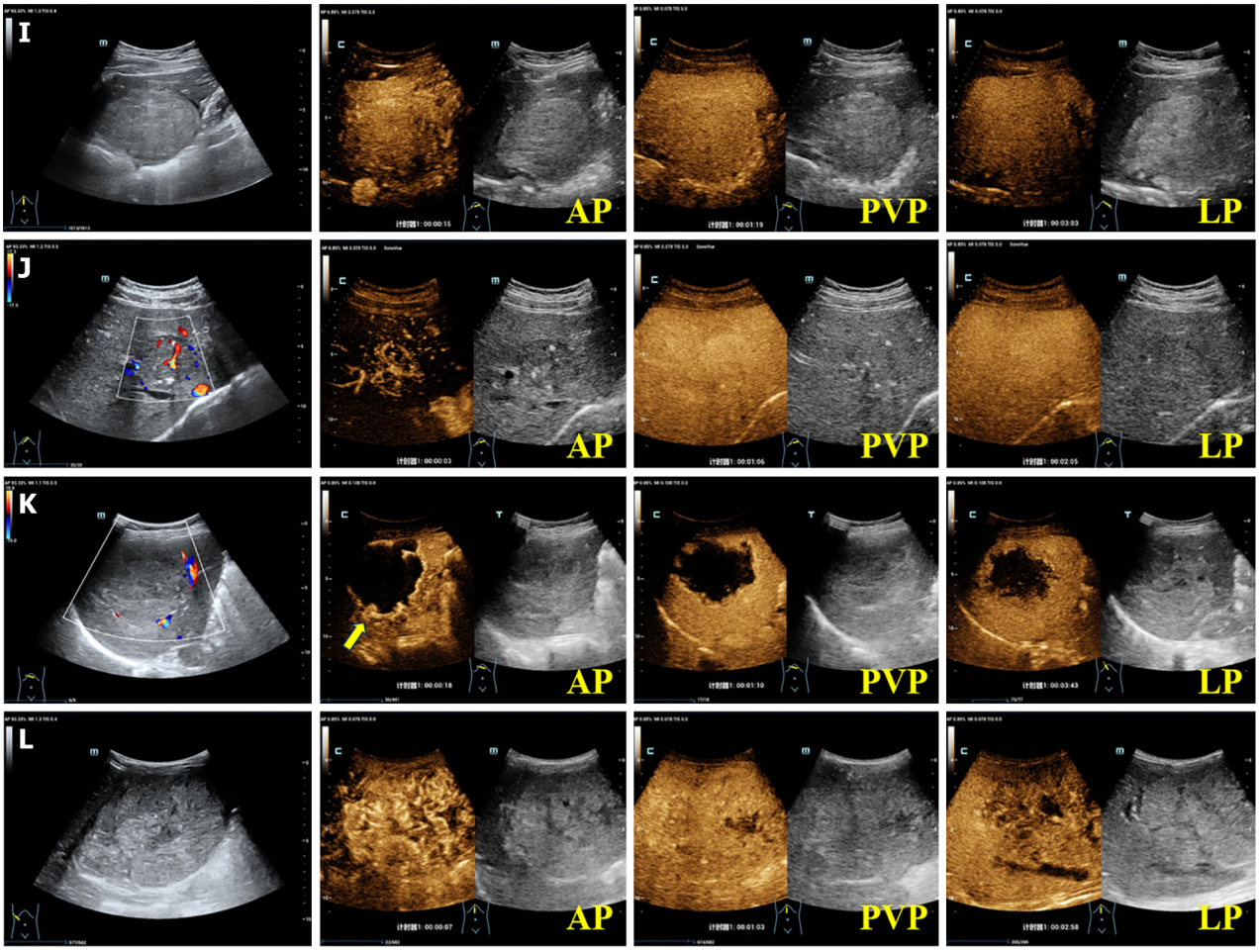


Figure 5 Contrast-enhanced ultrasound images of solid focal liver lesions. A: A 37-year-old female patient presenting with a lesion of hepatic cystic echinococcosis 4, revealing no enhancement in the arterial phase (AP), portal venous phase (PVP), and late phase (LP); B: A 30-year-old female patient presenting with a hailstorm hepatic alveolar echinococcosis lesion, exhibiting irregular mild hyper-enhancement around the periphery in the AP and hypo-enhancement in the PVP and LP, resembling a "worm-eaten" appearance, with no significant enhancement observed in most of the internal regions; C: A 49-year-old female patient presenting with a lesion consistent with paragonimiasis, exhibiting heterogeneous enhancement in the AP, with non-enhancing reticular and "tunnel-like" areas internally; D: A 70-year-old female patient presenting with a liver abscess, showing hyper-enhancement of the cystic wall and internal septa in the AP, with multiple patches of non-enhancing liquefied necrotic areas, creating a "honeycomb-like" pattern; E: A 73-year-old male patient presenting with a lesion from hepatocellular carcinoma, exhibiting heterogeneous hyper-enhancement in the AP, iso-enhancement in the PVP, and hypo-enhancement in the LP; F: A 36-year-old male patient presenting with a lesion indicative of intrahepatic cholangiocarcinoma, showing irregular "rim-like" peripheral enhancement in the AP (the yellow arrow), washout in the PVP, and significant hypo-enhancement in the LP; G: A 40-year-old male patient presenting with liver metastasis, showing thick "rim-like" hyper-enhancement in the early AP (the yellow arrow), with washout in the early PVP and marked hypo-enhancement in the LP, presenting as a "bull's eye" sign; H: A 57-year-old female patient presenting with hepatic biliary cystadenoma. The lesion shows slight enhancement of the wall and septa in the AP, with some areas exhibiting thickened septa and dense nodular enhancement, followed by decreased enhancement in the PVP and LP; I: A 14-year-old female patient presenting with hepatocellular adenoma. The lesion shows slight hyper-enhancement in the AP and LP, and iso-enhancement in the LP; J: A 23-year-old male patient presenting with a lesion consistent with focal nodular hyperplasia, characterized by centrifugal enhancement in a "spoke-wheel" or "firework-like" pattern extending from the center to the periphery in the AP. The lesion shows slight hyper-enhancement in the PVP, and iso-enhancement in the LP; K: A 57-year-old female patient presenting with hepatic sclerosing hemangioma. The lesion shows discontinuous, nodular peripheral enhancement in the AP (the yellow arrow), with progressive partial or complete centripetal fill-in in the PVP and slight hyper-enhancement in the LP, as well as patchy non-enhancing areas observed internally; L: A 2-year-old male patient presenting with a lesion associated with hepatoblastoma, showing hyper-enhancement in the AP, slight hypo-enhancement in the PVP, and hypo-enhancement in the LP.

are often multifocal, and typical metastatic lesions manifest as single or multiple hyperechoic masses surrounded by hypoechoic edema and internal necrotic hypoechoic areas, presenting as the "bull's eye" sign. These lesions demonstrate thick, "rim-like" hyperenhancement in the AP, followed by early washout and significant hypoenhancement in the LP (Figure 5G)[25,50,56]. Liver metastases need to be distinguished from metastasis-like HAE lesions; (6) Hepatic biliary cystadenoma exhibits a multilocular structure with solid mural nodules protruding into the lumen. Mild enhancement can be observed in the cyst walls, internal septations, and mural nodules (Figure 5H)[57]. Hepatobiliary cystadenomas need to be differentiated from HCE2, HCE3, and pseudocystic HAE lesions; (7) Hepatocellular adenoma is a rare benign liver tumor that typically appears as a well-defined, homogeneously echoic mass. A typical contrast-enhanced appearance included uniform hyperenhancement in the AP, followed by isoenhancement or hypoenhancement in the PVP and LP (Figure 5I). Non-enhancing areas may be observed in cases of hemorrhagic necrosis[50,55,58]; (8) Hepatic focal nodular hyperplasia typically manifests as an isoechoic mass with central stellate fibrotic scar tissue within the internal region. Approximately 70% of cases demonstrate a centrifugal enhancement pattern, with a spokewheel or

firework-like enhancement radiating from the center to the periphery of the AP. In the PVP and LP, the lesion exhibits isoenhancement or slight hyperenhancement, whereas the central scar remains unenhanced (Figure 5J)[50,55,58]; (9) The hepatic hemangioma is the second most common benign FLL. It most frequently manifests as a well-defined highly echogenic mass with a reticular internal pattern. Typically, hemangiomas demonstrate discontinuous nodular enhancement at the periphery in the AP, followed by gradual centripetal filling in the PVP and isoenhancement or slight hyperenhancement in the LP. In cases of hepatic sclerosing hemangiomas, intratumoral thrombosis may result in large non-enhancing areas within the lesion (Figure 5K)[26,50]; and (10) Hepatoblastoma is the most common liver malignancy in children. Hepatoblastoma presents as a well-defined heterogeneously echoic mass with visible areas of liquefactive necrosis. CEUS revealed hyperenhancement in the AP, followed by washout in the PVP and hypoenhancement in the parenchymal phase. Liquefactive necrotic areas remain unenhanced (Figure 5L)[59,60].

Based on CEUS, it is possible to differentiate HAE lesions from other FLLs that share some overlapping features. Although lesions of HAE, ICC, and liver metastases all exhibit ring-like enhancement on CEUS, the key to differentiation lies in the specific patterns observed: ICC lesions show irregular or "lace-like" enhancement within the lesions, liver metastases exhibit "thick ring-like" enhancement within the lesions, while HAE lesions demonstrate "ring-like" enhancement around the lesion periphery. The washout of enhancement in ICC and liver metastases is significantly faster than in HAE. The scoring system proposed by Wa *et al*[39] can accurately distinguish between HAE and ICC with a sensitivity and specificity of 80.0% and 81.3%, respectively. Additionally, on conventional ultrasound, liver metastases typically exhibit central hypoechoic necrosis, while metastasis-like HAE lesions often have a central punctate scar, which also aids in differentiation.

Pseudocystic HAE lesions need to be differentiated from hepatic biliary cystadenomas and mature liver abscesses. On CEUS, pseudocystic HAE lesions mostly lack internal enhancement, while hepatic biliary cystadenomas show enhancement of intraluminal nodules and internal septations within the lesions. Mature liver abscesses exhibit enhancement of both the cyst wall and internal septations, presenting a "honeycomb-like" pattern. Hemangioma-like HAE lesions need to be differentiated from the hepatic sclerosing hemangiomas, the later of which can be characterized by early arterial bulbous ring enhancement and iris diaphragm phenomenon within the lesions.

OTHER IMAGING MODALITIES FOR THE DIAGNOSIS OF HEPATIC ECHINOCOCCOSIS AND FUTURE RESEARCH DIRECTIONS

Different imaging modalities offer unique advantages. Ultrasonography offers convenient and clear visualization of the lesion matrix and cyst walls. Compared with preoperative ultrasound and CT, IOUS is the most effective method to detect the relationship between the outer capsule of HCE and blood vessels, as well as distinguishing between CE3b and CE4. The use of IOUS can prevent recurrence and reduce postoperative morbidity[61].

CT and MRI have the advantages of multiparameter and high-resolution imaging, enabling multidirectional visualization of the adjacent relationships between lesions and hepatic blood vessels as well as the intrahepatic bile ducts[30,62,63]. CT is highly sensitive in detecting calcification in hepatic echinococcosis. The HAE lesions exhibit characteristic high-signal intensity "small vesicles/vesicle nests" on T2-weighted imaging. Diffusion-weighted imaging reveals a slightly hyperintense "infiltration zone" or "halo sign" surrounding the lesion, whereas the parenchyma typically exhibits no diffusion restriction, with a high apparent diffusion coefficient value on diffusion-weighted imaging sequences. This is an important criterion for differentiating HAE from hepatic malignancies[23,64].

An assessment of lesion activity using fluorodeoxyglucose-positron emission tomography (FDG-PET) is a recognized standard that reflects the metabolic activity of HAE lesions through FDG uptake induced by the immune responses surrounding the lesion. Some studies have indicated that MRI, CT, and CEUS can be utilized to assess the activity of HAE lesions by observing typical microcystic structures, microcalcifications, or blood supply to these lesions that are associated with high metabolic activity on FDG-PET[65-68].

Recent advances in artificial intelligence have significantly enhanced the diagnostic accuracy of hepatic echinococcosis. Yang *et al*[69] trained and validated a deep convolutional neural network model that exhibited a significantly better performance than senior radiologists in highly endemic areas (area under the receiver operating characteristic curve 0.942 *vs* 0.844; $P = 0.027$). Additionally, this model improved the diagnostic capabilities of junior radiologists (area under the receiver operating characteristic curve from 0.743 to 0.850; $P < 0.05$) for hepatic echinococcosis in both high-endemic and remote areas, demonstrating great potential for future development and clinical value.

In the future, the CEUS classification should be further developed, with an emphasis on lesion activity. Building on previous research[35,47,69], future work should focus on comparing superb microvascular imaging with CEUS to quantitatively assess the degree of vascularization in HAE. Additionally, exploring the integration of *Echinococcosis multilocularis* Ulm classification into the evolution scheme, and using artificial intelligence to classify various subtypes of hepatic echinococcosis could enhance diagnostic accuracy and patient management.

CONCLUSION

Diagnosing hepatic echinococcosis is challenging and often relies on a combination of medical history, serology, and imaging techniques. Ultrasonography is the preferred screening method in endemic regions. Therefore, for radiologists in endemic areas, accurately determining the ultrasonic characteristics of different types of hepatic echinococcosis is crucial

to improve diagnostic accuracy. The typical ultrasonographic features of HCE include the "double-wall", "daughter cysts", "water lily", and "cerebral gyrus" signs, whereas HAE often manifests as solid masses with ill-defined boundaries, possibly accompanied by calcification or liquefied cavities. CEUS can reveal the characteristic "black hole sign" of hepatic echinococcosis lesions, which is instrumental in differentiating these lesions from other FLLs. With the continuous advancement in technology, integrating sophisticated artificial intelligence software with ultrasound equipment is expected to significantly enhance the diagnostic accuracy of hepatic echinococcosis in endemic areas, thereby offering a vast potential for further development.

ACKNOWLEDGEMENTS

We extend our heartfelt gratitude to the Department of Medical Ultrasound of West China Hospital, Sichuan University, for providing invaluable data for this review.

FOOTNOTES

Author contributions: Tao Y and Wang YF collected and screened clinical cases; Tao Y drafted the initial manuscript; Wang YF was responsible for subsequent manuscript revisions; Wang J and Seyler BC assisted in refining the English quality of the article and participated in manuscript revisions; Long S provided radiological expertise; Zhong XF meticulously reverified the conventional, contrast-enhanced, and intraoperative ultrasound images for publication; Lu Q conceived and designed the protocol, oversaw the overall design, supervised the study, and revised the manuscript.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Country of origin: China

ORCID number: Yi Tao 0000-0002-8273-4328; Yi-Fei Wang 0000-0002-3908-1026; Qiang Lu 0000-0002-4057-1997.

S-Editor: Wang JJ
L-Editor: A
P-Editor: Yu HG

REFERENCES

1 **McManus DP**, Gray DJ, Zhang W, Yang Y. Diagnosis, treatment, and management of echinococcosis. *BMJ* 2012; **344**: e3866 [PMID: 22689886 DOI: 10.1136/bmj.e3866]
2 **Wen H**, Vuitton L, Tuxun T, Li J, Vuitton DA, Zhang W, McManus DP. Echinococcosis: Advances in the 21st Century. *Clin Microbiol Rev* 2019; **32** [PMID: 30760475 DOI: 10.1128/CMR.00075-18]
3 **Schweiger A**, Ammann RW, Candinas D, Clavien PA, Eckert J, Gottstein B, Halkic N, Muellhaupt B, Prinz BM, Reichen J, Tarr PE, Torgerson PR, Deplazes P. Human alveolar echinococcosis after fox population increase, Switzerland. *Emerg Infect Dis* 2007; **13**: 878-882 [PMID: 17553227 DOI: 10.3201/eid1306.061074]
4 **Wang X**, Dai G, Li M, Jia W, Guo Z, Lu J. Prevalence of human alveolar echinococcosis in China: a systematic review and meta-analysis. *BMC Public Health* 2020; **20**: 1105 [PMID: 32664905 DOI: 10.1186/s12889-020-08989-8]
5 **Zhang W**, Zhang Z, Wu W, Shi B, Li J, Zhou X, Wen H, McManus DP. Epidemiology and control of echinococcosis in central Asia, with particular reference to the People's Republic of China. *Acta Trop* 2015; **141**: 235-243 [PMID: 24686096 DOI: 10.1016/j.actatropica.2014.03.014]
6 **Li B**, Quzhen G, Xue CZ, Han S, Chen WQ, Yan XL, Li ZJ, Quick ML, Huang Y, Xiao N, Wang Y, Wang LY, Zuoga G, Bianba, Gangzhu, Ma BC, Gasong, Wei XG, Niji, Zheng CJ, Wu WP, Zhou XN. Epidemiological survey of echinococcosis in Tibet Autonomous Region of China. *Infect Dis Poverty* 2019; **8**: 29 [PMID: 31030673 DOI: 10.1186/s40249-019-0537-5]
7 **Wang LY**, Qin M, Liu ZH, Wu WP, Xiao N, Zhou XN, Manguin S, Gavotte L, Frutos R. Prevalence and spatial distribution characteristics of human echinococcosis in China. *PLoS Negl Trop Dis* 2021; **15**: e0009996 [PMID: 34962928 DOI: 10.1371/journal.pntd.0009996]
8 **Ma T**, Jiang D, Quzhen G, Xue C, Han S, Wu W, Zheng C, Ding F. Factors influencing the spatial distribution of cystic echinococcosis in Tibet, China. *Sci Total Environ* 2021; **754**: 142229 [PMID: 33254864 DOI: 10.1016/j.scitotenv.2020.142229]
9 **Wang Q**, Yang L, Wang Y, Zhang GJ, Zhong B, Wu WP, Zheng CJ, Liao S, Yu WJ, He W, Wang Q, Chen F, Li RR, Huang Y, Yao R, Zhou XN. Disease burden of echinococcosis in Tibetan communities-A significant public health issue in an underdeveloped region of western China. *Acta Trop* 2020; **203**: 105283 [PMID: 31811863 DOI: 10.1016/j.actatropica.2019.105283]
10 **Fu MH**, Wang X, Han S, Guan YY, Bergquist R, Wu WP. Advances in research on echinococcoses epidemiology in China. *Acta Trop* 2021; **219**: 105921 [PMID: 33878307 DOI: 10.1016/j.actatropica.2021.105921]
11 **He W**, Wang LY, Yu WJ, Zhang GJ, Zhong B, Liao S, Wang Q, Li RR, Yang L, Yao RX, Liu Y, Danba Z, Qin SC, Wang SA, Wang YX,

Huang Y, Wang Q. Prevalence and spatial distribution patterns of human echinococcosis at the township level in Sichuan Province, China. *Infect Dis Poverty* 2021; **10**: 82 [PMID: 34090538 DOI: 10.1186/s40249-021-00862-z]

12 **Cai H**, Guan Y, Ma X, Wang L, Wang H, Su G, Zhang X, Han X, Ma J, Liu YF, Li J, Zhang J, Wang Y, Wang W, Du R, Lei W, Wu W. Epidemiology of Echinococcosis Among Schoolchildren in Golog Tibetan Autonomous Prefecture, Qinghai, China. *Am J Trop Med Hyg* 2017; **96**: 674-679 [PMID: 28070013 DOI: 10.4269/ajtmh.16-0479]

13 **Han XM**, Cai QG, Wang W, Wang H, Zhang Q, Wang YS. Childhood suffering: hyper endemic echinococcosis in Qinghai-Tibetan primary school students, China. *Infect Dis Poverty* 2018; **7**: 71 [PMID: 29996900 DOI: 10.1186/s40249-018-0455-y]

14 **Wang L**, Gongsang Q, Pang H, Qin M, Wang Y, Li J, Frutos R, Gavotte L. Assessment of echinococcosis control in Tibet Autonomous Region, China. *Infect Dis Poverty* 2022; **11**: 59 [PMID: 35619124 DOI: 10.1186/s40249-022-00987-9]

15 **Fu M**, Han S, Xue C, Wang X, Liu B, Wang Y, Wang L, Wei S, Cui X, Zhang T, Zhang HB, Zheng B, Tian T, Yang S, Gao CH, Dang Z, Xu B, Yu Q, Wu W. Contribution to the echinococcosis control programme in China by NIPD-CTDR. *Adv Parasitol* 2020; **110**: 107-144 [PMID: 32563323 DOI: 10.1016/bs.apar.2020.04.010]

16 **Qucuo N**, Wu G, He R, Quzhen D, Zhuoga C, Deji S, Zhang L, Zhao Z, Du Z. Knowledge, attitudes and practices regarding echinococcosis in Xizang Autonomous Region, China. *BMC Public Health* 2020; **20**: 483 [PMID: 32293375 DOI: 10.1186/s12889-020-8314-8]

17 **Kui Y**, Liu B, Wang X, Xue C, Xue J, Zhang Y, Zhang B, Dai Y, Han S, Wu W. Epidemiological Characteristics of Echinococcosis in Non-Endemic PLADs - China, 2017-2020. *China CDC Wkly* 2021; **3**: 1084-1088 [PMID: 34938586 DOI: 10.46234/ccdcw2021.262]

18 **Paternoster G**, Boo G, Wang C, Minbaeva G, Usubalieva J, Raimkulov KM, Zhoroev A, Abdykerimov KK, Kronenberg PA, Müllhaupt B, Furrer R, Deplazes P, Torgerson PR. Epidemic cystic and alveolar echinococcosis in Kyrgyzstan: an analysis of national surveillance data. *Lancet Glob Health* 2020; **8**: e603-e611 [PMID: 32199126 DOI: 10.1016/S2214-109X(20)30038-3]

19 **Zi JR**, Xiao D, Peng J, Wu FW, Li JX, Yan XL, Wang ZQ, Cai X, Xu Q, Li BF, Yang YM. Epidemiological survey of cystic echinococcosis in southwest China: From the Qinghai-Tibet plateau to the area of Yunnan. *World J Hepatol* 2024; **16**: 229-240 [PMID: 38495269 DOI: 10.4254/wjh.v16.i2.229]

20 **Schuhbaur J**, Schweizer M, Philipp J, Schmidberger J, Schlingeloff P, Kratzer W. Long-term follow-up of liver alveolar echinococcosis using echinococcosis multilocularis ultrasound classification. *World J Gastroenterol* 2021; **27**: 6939-6950 [PMID: 34790016 DOI: 10.3748/wjg.v27.i40.6939]

21 **Brunetti E**, Kern P, Vuitton DA; Writing Panel for the WHO-IWGE. Expert consensus for the diagnosis and treatment of cystic and alveolar echinococcosis in humans. *Acta Trop* 2010; **114**: 1-16 [PMID: 19931502 DOI: 10.1016/j.actatropica.2009.11.001]

22 **Liu W**, Delabrousse É, Blagosklonov O, Wang J, Zeng H, Jiang Y, Wang J, Qin Y, Vuitton DA, Wen H. Innovation in hepatic alveolar echinococcosis imaging: best use of old tools, and necessary evaluation of new ones. *Parasite* 2014; **21**: 74 [PMID: 25531446 DOI: 10.1051/parasite/2014072]

23 **Kantarci M**, Bayraktutan U, Karabulut N, Aydinli B, Ogul H, Yuce I, Calik M, Eren S, Atamanalp SS, Oto A. Alveolar echinococcosis: spectrum of findings at cross-sectional imaging. *Radiographics* 2012; **32**: 2053-2070 [PMID: 23150858 DOI: 10.1148/rg.327125708]

24 **Ma T**, Jiang D, Hao M, Fan P, Zhang S, Quzhen G, Xue C, Han S, Wu W, Zheng C, Ding F. Geographical Detector-based influence factors analysis for Echinococcosis prevalence in Tibet, China. *PLoS Negl Trop Dis* 2021; **15**: e0009547 [PMID: 34252103 DOI: 10.1371/journal.pntd.0009547]

25 **Schweizer M**, Schmidberger J, Schlingeloff P, Kratzer W. Contrast-enhanced ultrasound (CEUS) in patients with metastasis-like hepatic alveolar echinococcosis: a cohort study. *J Ultrasound* 2023; **26**: 129-136 [PMID: 35597873 DOI: 10.1007/s40477-022-00688-x]

26 **Philipp J**, Schmidberger J, Schlingeloff P, Kratzer W. Differentiation of hepatic alveolar echinococcosis with a hemangioma-like pattern compared to typical liver hemangioma using contrast-enhanced ultrasound: a pilot study. *Infection* 2023; **51**: 159-168 [PMID: 35776381 DOI: 10.1007/s15010-022-01866-z]

27 **Graeter T**, Ehing F, Oeztuerk S, Mason RA, Haenle MM, Kratzer W, Seufferlein T, Gruener B. Hepatobiliary complications of alveolar echinococcosis: A long-term follow-up study. *World J Gastroenterol* 2015; **21**: 4925-4932 [PMID: 25945006 DOI: 10.3748/wjg.v21.i16.4925]

28 **Frei P**, Misselwitz B, Prakash MK, Schoepfer AM, Prinz Vavricka BM, Müllhaupt B, Fried M, Lehmann K, Ammann RW, Vavricka SR. Late biliary complications in human alveolar echinococcosis are associated with high mortality. *World J Gastroenterol* 2014; **20**: 5881-5888 [PMID: 24914349 DOI: 10.3748/wjg.v20.i19.5881]

29 **Tao S**, Qin Z, Hao W, Yongquan L, Lanhui Y, Lei Y. Usefulness of gray-scale contrast-enhanced ultrasonography (SonoVue®) in diagnosing hepatic alveolar echinococcosis. *Ultrasound Med Biol* 2011; **37**: 1024-1028 [PMID: 21640477 DOI: 10.1016/j.ultrasmedbio.2011.04.014]

30 **Chinese Doctor Association**, Chinese College of Surgeons; Chinese Committee for Hydatidology (CCH). [Expert consensus on diagnosis and treatment of hepatic cystic and alveolar echinococcosis (2019 edition)]. *Zhonghua Xiaohua Waike Zazhi* 2019; **18**: 711-721 [DOI: 10.3760/cma.j.issn.1673-9752.2019.08.002]

31 **WHO Informal Working Group**. International classification of ultrasound images in cystic echinococcosis for application in clinical and field epidemiological settings. *Acta Trop* 2003; **85**: 253-261 [PMID: 12606104 DOI: 10.1016/s0001-706x(02)00223-1]

32 **Radiology of infection Sub-branch**, Radiology Branch; Chinese Medical Association; Committee on Radiology of infectious, Radiology Branch, Chinese Medical Doctor Association. [Expert consensus on the imaging diagnosis of hepatic echinococcosis]. *Linchuang Gandanbing Zazhi* 2021; **37**: 792-797 [DOI: 10.3969/j.issn.1001-5256.2021.04.014]

33 **Kern P**, Wen H, Sato N, Vuitton DA, Gruener B, Shao Y, Delabrousse E, Kratzer W, Bresson-Hadni S. WHO classification of alveolar echinococcosis: principles and application. *Parasitol Int* 2006; **55** Suppl: S283-S287 [PMID: 16343985 DOI: 10.1016/j.parint.2005.11.041]

34 **Grimm J**, Beck A, Nell J, Schmidberger J, Hillenbrand A, Beer AJ, Dezsényi B, Shi R, Beer M, Kern P, Henne-Bruns D, Kratzer W, Moller P, Barth TF, Gruener B, Graeter T. Combining Computed Tomography and Histology Leads to an Evolutionary Concept of Hepatic Alveolar Echinococcosis. *Pathogens* 2020; **9** [PMID: 32759781 DOI: 10.3390/pathogens9080634]

35 **Graeter T**, Schmidberger J. Stage-Oriented CT Classification and Intermodal Evolution Model in Hepatic Alveolar Echinococcosis. *Rofo* 2022; **194**: 532-544 [PMID: 35081647 DOI: 10.1055/a-1710-3669]

36 **Kodama Y**, Fujita N, Shimizu T, Endo H, Nambu T, Sato N, Todo S, Miyasaka K. Alveolar echinococcosis: MR findings in the liver. *Radiology* 2003; **228**: 172-177 [PMID: 12750459 DOI: 10.1148/radiol.2281020323]

37 **Graeter T**, Bao HH, Shi R, Liu WY, Li WX, Jiang Y, Schmidberger J, Brumpt E, Delabrousse E, Kratzer W; XUUB Consortium. Evaluation of intrahepatic manifestation and distant extrahepatic disease in alveolar echinococcosis. *World J Gastroenterol* 2020; **26**: 4302-4315 [PMID: 32848335 DOI: 10.3748/wjg.v26.i29.4302]

38 **Kratzer W**, Gruener B, Kaltenbach TE, Ansari-Bitzenberger S, Kern P, Fuchs M, Mason RA, Barth TF, Haenle MM, Hillenbrand A, Oeztuerk S, Graeter T. Proposal of an ultrasonographic classification for hepatic alveolar echinococcosis: Echinococcosis multilocularis Ulm

classification-ultrasound. *World J Gastroenterol* 2015; **21**: 12392-12402 [PMID: 26604646 DOI: 10.3748/wjg.v21.i43.12392]

39 **Wa ZC**, Du T, Li XF, Xu HQ, Suo-Ang QC, Chen LD, Hu HT, Wang W, Lu MD. Differential diagnosis between hepatic alveolar echinococcosis and intrahepatic cholangiocarcinoma with conventional ultrasound and contrast-enhanced ultrasound. *BMC Med Imaging* 2020; **20**: 101 [PMID: 32854653 DOI: 10.1186/s12880-020-00499-8]

40 **Zhang X**, Suolang L, Ren Y, Wang Y, Jiang Y, Zhong X, Gou Z, Zhou W, Chen J, Li Y, Cai D. Can contrast-enhanced ultrasound differentiate the type of hepatic echinococcosis: cystic echinococcosis or alveolar echinococcosis? *Parasit Vectors* 2023; **16**: 131 [PMID: 37069610 DOI: 10.1186/s13071-023-05731-2]

41 **Schwarze V**, Mueller-Peltzer K, Negrão de Figueiredo G, Lindner F, Rübenthaler J, Clevert DA. The use of contrast-enhanced ultrasound (CEUS) for the diagnostic evaluation of hepatic echinococcosis. *Clin Hemorheol Microcirc* 2018; **70**: 449-455 [PMID: 30347607 DOI: 10.3233/CH-189310]

42 **Zhang H**, Liu ZH, Zhu H, Han Y, Liu J, Deng LQ. Analysis of contrast-enhanced ultrasound (CEUS) and pathological images of hepatic alveolar echinococcosis (HAE) lesions. *Eur Rev Med Pharmacol Sci* 2016; **20**: 1954-1960 [PMID: 27249592]

43 **Cai DM**, Wang HY, Wang XL, Jiang Y, Luo Y, Li YZ. Ultrasonographic findings of small lesion of hepatic alveolar echinococcosis. *Acta Trop* 2017; **174**: 165-170 [PMID: 26892870 DOI: 10.1016/j.actatropica.2016.01.030]

44 **Cai D**, Li Y, Jiang Y, Wang H, Wang X, Song B. The role of contrast-enhanced ultrasound in the diagnosis of hepatic alveolar echinococcosis. *Medicine (Baltimore)* 2019; **98**: e14325 [PMID: 30702614 DOI: 10.1097/MD.0000000000014325]

45 **Jiang Y**, Li J, Wang J, Xiao H, Li T, Liu H, Liu W. Assessment of Vascularity in Hepatic Alveolar Echinococcosis: Comparison of Quantified Dual-Energy CT with Histopathologic Parameters. *PLoS One* 2016; **11**: e0149440 [PMID: 26901164 DOI: 10.1371/journal.pone.0149440]

46 **Zeng H**, Wang J, Xie W, Liu W, Wen H. Assessment of early hepatic echinococcus multilocularis infection in rats with real-time contrast-enhanced ultrasonography. *Ultrasound Med Biol* 2012; **38**: 1982-1988 [PMID: 22929653 DOI: 10.1016/j.ultrasmedbio.2012.07.007]

47 **Kratzer W**, Güthle M, Dobler F, Seufferlein T, Graeter T, Schmidberger J, Barth TF, Klaus J. Comparison of superb microvascular imaging (SMI) quantified with ImageJ to quantified contrast-enhanced ultrasound (qCEUS) in liver metastases-a pilot study. *Quant Imaging Med Surg* 2022; **12**: 1762-1774 [PMID: 35284256 DOI: 10.21037/qims-21-383]

48 **Stojkovic M**, Mickan C, Weber TF, Junghanss T. Pitfalls in diagnosis and treatment of alveolar echinococcosis: a sentinel case series. *BMJ Open Gastroenterol* 2015; **2**: e000036 [PMID: 26462284 DOI: 10.1136/bmjgast-2015-000036]

49 **Kim TH**, Yoon JH, Lee JM. Emerging Role of Hepatobiliary Magnetic Resonance Contrast Media and Contrast-Enhanced Ultrasound for Noninvasive Diagnosis of Hepatocellular Carcinoma: Emphasis on Recent Updates in Major Guidelines. *Korean J Radiol* 2019; **20**: 863-879 [PMID: 31132813 DOI: 10.3348/kjr.2018.0450]

50 **Dietrich CF**, Nolsøe CP, Barr RG, Berzigotti A, Burns PN, Cantisani V, Chammas MC, Chaubal N, Choi BI, Clevert DA, Cui X, Dong Y, D'Onofrio M, Fowlkes JB, Gilja OH, Huang P, Ignee A, Jenssen C, Kono Y, Kudo M, Lassau N, Lee WJ, Lee JY, Liang P, Lim A, Lyshchik A, Meloni MF, Correas JM, Minami Y, Moriyasu F, Nicolau C, Piscaglia F, Saftoiu A, Sidhu PS, Sporea I, Torzilli G, Xie X, Zheng R. Guidelines and Good Clinical Practice Recommendations for Contrast-Enhanced Ultrasound (CEUS) in the Liver-Update 2020 WFUMB in Cooperation with EFSUMB, AFSUMB, AIUM, and FLAUS. *Ultrasound Med Biol* 2020; **46**: 2579-2604 [PMID: 32713788 DOI: 10.1016/j.ultrasmedbio.2020.04.030]

51 **Lu Q**, Ling WW, Ma L, Huang ZX, Lu CL, Luo Y. Contrast-enhanced ultrasonographic findings of hepatic paragonimiasis. *World J Gastroenterol* 2013; **19**: 2087-2091 [PMID: 23599629 DOI: 10.3748/wjg.v19.i13.2087]

52 **Zarzour JG**, Porter KK, Tchelepi H, Robbin ML. Contrast-enhanced ultrasound of benign liver lesions. *Abdom Radiol (NY)* 2018; **43**: 848-860 [PMID: 29167944 DOI: 10.1007/s00261-017-1402-2]

53 **Fraquelli M**, Nadarevic T, Colli A, Manzotti C, Giljaca V, Miletic D, Štimac D, Casazza G. Contrast-enhanced ultrasound for the diagnosis of hepatocellular carcinoma in adults with chronic liver disease. *Cochrane Database Syst Rev* 2022; **9**: CD013483 [PMID: 36053210 DOI: 10.1002/14651858.CD013483.pub2]

54 **Guo HL**, Zheng X, Cheng MQ, Zeng D, Huang H, Xie XY, Lu MD, Kuang M, Wang W, Xian MF, Chen LD. Contrast-Enhanced Ultrasound for Differentiation Between Poorly Differentiated Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma. *J Ultrasound Med* 2022; **41**: 1213-1225 [PMID: 34423864 DOI: 10.1002/jum.15812]

55 **Dobek A**, Kobierecki M, Ciesielski W, Grząsiak O, Fabisiak A, Stefańczyk L. Usefulness of Contrast-Enhanced Ultrasound in the Differentiation between Hepatocellular Carcinoma and Benign Liver Lesions. *Diagnostics (Basel)* 2023; **13** [PMID: 37370920 DOI: 10.3390/diagnostics13122025]

56 **Sun L**, Yin S, Xing B, Li Z, Fan Z, Yan K. Contrast-Enhanced Ultrasound With SonoVue and Sonazoid for the Diagnosis of Colorectal Liver Metastasis After Chemotherapy. *J Ultrasound Med* 2023; **42**: 355-362 [PMID: 35734885 DOI: 10.1002/jum.16042]

57 **Dong Y**, Wang WP, Mao F, Fan M, Ignee A, Serra C, Sparchez Z, Sporea I, Braden B, Dietrich CF. Contrast enhanced ultrasound features of hepatic cystadenoma and hepatic cystadenocarcinoma. *Scand J Gastroenterol* 2017; **52**: 365-372 [PMID: 27887203 DOI: 10.1080/00365521.2016.1259652]

58 **Myers L**, Ahn J. Focal Nodular Hyperplasia and Hepatic Adenoma: Evaluation and Management. *Clin Liver Dis* 2020; **24**: 389-403 [PMID: 32620279 DOI: 10.1016/j.cld.2020.04.013]

59 **Anupindi SA**, Biko DM, Ntoulia A, Poznick L, Morgan TA, Darge K, Back SJ. Contrast-enhanced US Assessment of Focal Liver Lesions in Children. *Radiographics* 2017; **37**: 1632-1647 [PMID: 29019750 DOI: 10.1148/rg.2017170073]

60 **McCarville MB**. Contrast-enhanced sonography in pediatrics. *Pediatr Radiol* 2011; **41** Suppl 1: S238-S242 [PMID: 21523607 DOI: 10.1007/s00247-011-2005-7]

61 **Trigui A**, Toumi N, Fendri S, Saumtally MS, Zribi I, Akrout A, Mzali R, Ketata S, Dziri C, Amar MB, Boujelbene S. Cystic Echinococcosis of the Liver: Correlation Between Intra-Operative Ultrasound and Pre-Operative Imaging. *Surg Infect (Larchmt)* 2024; **25**: 213-220 [PMID: 38483340 DOI: 10.1089/sur.2023.335]

62 **Yu XK**, Zhang L, Ma WJ, Bi WZ, Ju SG. An Overview of Hepatic Echinococcosis and the Characteristic CT and MRI Imaging Manifestations. *Infect Drug Resist* 2021; **14**: 4447-4455 [PMID: 34737585 DOI: 10.2147/IDR.S331957]

63 **Calame P**, Weck M, Busse-Cote A, Brumpt E, Richou C, Turco C, Doussot A, Bresson-Hadni S, Delabrousse E. Role of the radiologist in the diagnosis and management of the two forms of hepatic echinococcosis. *Insights Imaging* 2022; **13**: 68 [PMID: 35394226 DOI: 10.1186/s13244-022-01190-y]

64 **Kantarci M**, Pirimoglu B. Diffusion-weighted MR imaging findings in a growing problem: hepatic alveolar echinococcosis. *Eur J Radiol* 2014; **83**: 1991-1992 [PMID: 25112672 DOI: 10.1016/j.ejrad.2014.07.013]

65 **Li J**, Dong J, Yang L, Li X, Song T. Comparison of [(18)F]Fluorodeoxyglucose Positron Emission Tomography and Contrast-Enhanced

Ultrasound for Evaluation of Hepatic Alveolar Echinococcosis Activity. *Ultrasound Med Biol* 2018; **44**: 2199-2208 [PMID: 30077410 DOI: 10.1016/j.ultrasmedbio.2018.06.010]

66 **Azizi A**, Blagosklonov O, Lounis A, Berthet L, Vuitton DA, Bresson-Hadni S, Delabrousse E. Alveolar echinococcosis: correlation between hepatic MRI findings and FDG-PET/CT metabolic activity. *Abdom Imaging* 2015; **40**: 56-63 [PMID: 24970734 DOI: 10.1007/s00261-014-0183-0]

67 **Brumpt E**, Blagosklonov O, Calame P, Bresson-Hadni S, Vuitton DA, Delabrousse E. AE hepatic lesions: correlation between calcifications at CT and FDG-PET/CT metabolic activity. *Infection* 2019; **47**: 955-960 [PMID: 31165442 DOI: 10.1007/s15010-019-01328-z]

68 **Kaltenbach TE**, Graeter T, Mason RA, Kratzer W, Oeztuerk S, Haenle MM, Gruener B, Gottstein M. Determination of vitality of liver lesions by alveolar echinococcosis. Comparison of parametric contrast enhanced ultrasound (SonoVue®) with quantified 18F-FDG-PET-CT. *Nuklearmedizin* 2015; **54**: 43-49 [PMID: 25423884 DOI: 10.3413/Nukmed-0670-14-05]

69 **Yang Y**, Cairang Y, Jiang T, Zhou J, Zhang L, Qi B, Ma S, Tang L, Xu D, Bu L, Bu R, Jing X, Wang H, Zhou Z, Zhao C, Luo B, Liu L, Guo J, Nima Y, Hua G, Wa Z, Zhang Y, Zhou G, Jiang W, Wang C, De Y, Yu X, Cheng Z, Han Z, Liu F, Dou J, Feng H, Wu C, Wang R, Hu J, Yang Q, Luo Y, Wu J, Fan H, Liang P, Yu J. Ultrasound identification of hepatic echinococcosis using a deep convolutional neural network model in China: a retrospective, large-scale, multicentre, diagnostic accuracy study. *Lancet Digit Health* 2023; **5**: e503-e514 [PMID: 37507196 DOI: 10.1016/S2589-7500(23)00091-2]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com