

# Evaluation and Classification of Incidentally Detected Splenic Lesions Based on B-Mode and Contrast-Enhanced Ultrasound

## Evaluation und Klassifikation von zufällig gefundenen Milzläsionen anhand von B-Mode- und kontrastmittelverstärktem Ultraschall

### Authors

Ehsan Safai Zadeh<sup>1</sup>, Christian Görg<sup>1</sup>, Clemens Post<sup>2</sup>, Amjad Alhyari<sup>1</sup>, Corinna Trenker<sup>3</sup>, Christoph F. Dietrich<sup>4</sup>, Hajo Findeisen<sup>5</sup>

### Affiliations

- 1 Interdisciplinary Center of Ultrasound Diagnostics; Gastroenterology, Endocrinology, Metabolism and Clinical Infectiology, Philipps-Universität Marburg, Marburg, Germany
- 2 Interdisciplinary Center of Ultrasound Diagnostics, University Hospital of Giessen and Marburg Campus Marburg, Marburg, Germany
- 3 Interdisciplinary Center of Ultrasound Diagnostics; Department of Hematology, University Hospital of Giessen and Marburg Campus Marburg, Marburg, Germany
- 4 Department General Internal Medicine, Hirslanden Beau Site, Salem and Permanence Clinics, Bern, Switzerland
- 5 Department for Internal Medicine, Red Cross Hospital Bremen, Bremen, Germany

### Key words

incidentaloma, methods & techniques, ultrasound, CEUS, diagnosis, splenic lesion

received 04.10.2022

accepted after revision 13.12.2022

published online 02.02.2023

### Bibliography

Ultraschall in Med 2023; 43: 637–644

DOI 10.1055/a-2001-5516

ISSN 0172-4614

© 2023, Thieme. All rights reserved.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

### Correspondence

Dr. Ehsan Safai Zadeh

Interdisciplinary Center of Ultrasound Diagnostics; Gastroenterology, Endocrinology, Metabolism and Clinical Infectiology, Philipps-Universität Marburg, Baldingerstraße, 35043 Marburg, Germany  
ehsan\_sz@yahoo.de

### ABSTRACT

**Purpose** To evaluate B-mode ultrasound (B-US) and contrast-enhanced ultrasound (CEUS) patterns of focal splenic incidentalomas (FSIs), and to correlate ultrasound patterns with benignity and malignancy via histologic examination and/or the clinical course.

**Materials and Methods** Between 2004 and 2021, 139 consecutive patients with an FSI detected by B-US were investigated additionally with CEUS. On CEUS, the arterial enhancement (AE) of the FSI (hyperenhancement, isoenhancement, hypoenhancement, and absent enhancement) was analyzed. Subsequently, the malignancy rate according to different B-US echo patterns and CEUS perfusion patterns was determined.

**Results** The final diagnosis of FSI was malignant in 9/139 (6.5%) and benign in 130/139 (93.5%) cases. The hypoechoic and hyperechoic lesions on B-US with arterial hyperenhancement on CEUS and the echogenic cystic or complex lesions on B-US with predominantly absent enhancement on CEUS were benign in 54/54 (100%) cases. 6/37 (16.2%) hypoechoic lesions on B-US with arterial hypo-/isoenhancement on CEUS and 3/48 (6.3%) of hyperechoic lesions on B-US with an arterial hypo-/isoenhancement on CEUS were malignant.

**Conclusion** Based on these results, FSIs reveal different malignancy rates depending on the B-US and CEUS patterns, and classification according to these B-US and CEUS patterns may be helpful in further evaluation of an FSI.

### ZUSAMMENFASSUNG

**Hintergrund** Evaluation von B-Mode-Ultraschall (B-US) und kontrastverstärktem Ultraschall (CEUS) von fokalen Milzinzidentalomen (FSI) und Korrelation der Ultraschallmuster mit der Dignität der Läsionen, gesichert durch histologische Untersuchung und/oder klinischen Verlauf.

**Materialien und Methoden** Zwischen 2004 und 2021 wurden 139 konsekutive Patienten mit einem durch B-US entdeckten FSI zusätzlich mit CEUS untersucht. Bei der CEUS wurde das arterielle Enhancement (AE) des FSI (Hyperenhancement, Isoenhancement, Hypoenhancement und fehlendes Enhancement) analysiert. Anschließend wurde die Malignitätsrate in Abhängigkeit von verschiedenen B-US-Echomustern und CEUS-Perfusionsmustern bestimmt.

**Ergebnisse** Die finale Diagnose zeigte maligne FSI in 9/139 (6,5 %) der Fälle und benigne FSI in 130/139 (93,5 %) der Fälle. Die im B-US echoreichen und echoarmen Läsionen und in der CEUS mit einem arteriellen Hyperenhancement sowie im B-US echogene, zystische oder komplexe Läsionen mit überwiegend fehlendem Enhancement in der CEUS waren zu 54/54 (100 %) benigne. 6/37 (16,2 %) der echoarmen Läsionen im

B-US mit arteriellem Hypo-/Isoenhancement in der CEUS und 3/48 (6,3 %) der echoreichen Läsionen im B-US mit arteriellem Hypo-/Isoenhancement in der CEUS waren maligne.

**Schlussfolgerung** FSI weisen je nach B-US- und CEUS-Muster unterschiedliche Malignitätsraten auf, und eine Klassifizierung anhand dieser Muster kann bei der weiteren Beurteilung eines FSI hilfreich sein.

## Introduction

In ancient times, the spleen was called the “organum plenum mysterii” before its function and significance were known [1]. Today, the spleen still does not receive much attention when evaluating imaging of the abdomen and is called the “forgotten organ” in the abdomen [2], since focal splenic pathologies are rare with a world population incidence of only up to 0.2 % [3]. In this context, incidental focal lesions of the spleen present a particular problem in everyday clinical practice, because an investigator’s personal experience with splenic pathologies is likely to be limited.

Due to a general reluctance to perform splenic biopsy, costly multimodality imaging is often requested for tumor characterization [4]. In the liver, contrast-enhanced ultrasound (CEUS) is the primary standard procedure for hepatic incidentalomas [5]. However, data are limited regarding the value of CEUS for the evaluation of incidental splenic lesion malignancy [6]. The aim of the present study was to evaluate B-mode ultrasound (B-US) and arterial CEUS perfusion patterns of focal splenic incidentalomas (FSIs), and to correlate US patterns with benignity and malignancy via histologic examination and/or clinical course.

## Patients and methods

Within the recruitment phase between 2004 and 2021, all patients with an FSI detected by B-US were investigated additionally with CEUS at our Interdisciplinary Center of Ultrasound Diagnostics (a tertiary healthcare facility at a university hospital), which is an ultrasound reference center for splenic pathologies. All lesions were examined by a single German Society for Ultrasound in Medicine (DEGUM) Level-III qualified examiner with more than 35 years of experience in the field of abdominal sonography (C.G. internal medicine) [7, 8]. FSIs were defined as asymptomatic and unexpected splenic lesions discovered incidentally on B-US, unrelated to the presenting illness, according to the World Federation for Ultrasound in Medicine and Biology position paper on incidental splenic findings [6]. Wedge-shaped subcapsular lesions with absent enhancement on CEUS that were diagnosed as splenic infarcts were not included in the study [9]. Furthermore, purely cystic anechoic lesions were not included in this study, because CEUS is not indicated in these cases.

During the specified period, approximately 285,000 sonographic examinations were performed in our ultrasound center, and 174 FSIs were found. The prevalence of splenic incidentalomas was approximately 0.06 %. This study was approved by the local ethics committee and conducted in accordance with the

amended Declaration of Helsinki. Informed consent for the US examination was obtained from each patient.

The inclusion criteria were 1) a solid round splenic lesion, an echogenic cystic splenic lesion, or a cystic splenic lesion with solid parts; 2) standardized documentation of B-US and CEUS examinations; 3) no relationship between the splenic lesion and the presenting illness of the patient, for which the investigation was performed; and 4) confirmation of the diagnosis of FSI by histologic examination and/or clinical and radiological follow-up.

In total, 35/174 patients (20.1 %) with an FSI were excluded: 32/35 (91.4 %) due to the absence of diagnostic confirmation regarding malignancy and benignity and 3/35 (8.6 %) due to the absence of standardized documentation of US examinations. Finally, data from 139 patients with an FSI were analyzed retrospectively.

## Classification of splenic incidentalomas based on medical history

According to the clinical background of the patients, the lesions were divided into two groups [10]:

1. *Splenic incidentalomas in a strict sense*: splenic lesions as incidental findings without known malignant disease;
2. *Splenic incidentalomas in an extended sense*: splenic lesions as incidental findings in patients with a prior history or current evidence of a malignant disease.

## Ultrasound examination

The B-US examinations were performed with an Acuson Sequoia 512 GI ultrasound machine (Siemens, Germany) and a 4C1 curved-array transducer with a frequency of 4 MHz.

The CEUS investigations were conducted with the same transducer in contrast-specific mode (1.5 MHz) and in accordance with the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines [7]. A bolus injection of 2.4 ml of the contrast medium SonoVue (Bracco Imaging S.p.A., Milan, Italy) was administered via peripheral venous access. This was followed by 10 ml of NaCl 0.9 %. For the first 30 seconds, the perfusion patterns of the lesions were continuously examined and recorded in a video clip. Subsequently, several short examinations were performed at 1-minute intervals for up to 3 minutes, and the changes in the perfusion pattern were saved as images. In patients with multiple lesions, the largest lesion was selected as the reference lesion. The following B-US and CEUS data were evaluated retrospectively.

## B-mode ultrasound

1. The echogenicity of the lesions was classified as hypoechoic, hyperechoic, echogenic cystic, or complex (cystic with solid parts) compared with the echogenicity of splenic parenchyma used as an *in vivo* reference [6, 11, 12].
2. The number of lesions was classified as solitary or multiple.
3. The size of lesions was measured in centimeters (maximum diameter).

## Contrast-enhanced ultrasound

1. The arterial enhancement (AE) of FSIs was categorized as hyper-enhancement, iso-enhancement, hypo-enhancement, or absent enhancement [2, 6, 11, 13]. The arterial phase was defined as the period from the earliest arrival of the contrast agent at the spleen until 60 seconds thereafter. Splenic tissue was considered as an *in vivo* reference to evaluate the AE of the contrast agent [14].

► **Table 1** Classification of incidental focal splenic lesions in the study patients (N = 139).

Group I	A	Hypoechoic on B-US and arterial hyper-enhancement on CEUS
	B	Hypoechoic on B-US and arterial iso-/hypo-enhancement on CEUS
Group II	A	Hyperechoic on B-US and arterial hyper-enhancement on CEUS
	B	Hyperechoic on B-US and arterial iso-/hypo-enhancement on CEUS
Group III	Echogenic cystic or complex on B-US and absent enhancement on CEUS	

B-US: B-mode ultrasound; CEUS: contrast-enhanced ultrasound

The B-US and CEUS data were evaluated retrospectively by two independent, experienced investigators (C.G., E.S.). In the event of discrepancies, the final decision was made by a third experienced investigator (H.F.).

## Classification of splenic lesions based on B-mode ultrasound and contrast-enhanced ultrasound patterns

After the B-US and CEUS examinations, the lesions were classified into five groups according to echogenicity on B-US (hypoechoic, hyperechoic, echogenic cystic, or complex) and arterial enhancement on CEUS (hyperenhancement, iso-enhancement, hypo-enhancement, or absent enhancement). The classification criteria were defined according to the modified classification of Bert and Görg et al. [11] (► **Table 1**).

## Statistical analysis

Statistical evaluation was performed on the categorical variable using Fisher's exact test and on continuous data using Mann-Whitney tests. Cohen's kappa statistics were applied to measure interrater reliability, and a *p*-value of <0.05 was defined as significant.

## Results

### Demographic and clinical data

Of the 139 patients, 73 were men and 66 were women. The average age was 56.5 years, with a range of 14–84 years. The final diagnosis was malignant FSI (mFSI) in 9/139 cases (6.5%) and benign FSI (bFSI) in 130/139 cases (93.5%). In total, the diagnosis was made by histologic confirmation in 18/139 cases (12.9%; 10 biopsies, 5 splenectomies, 3 autopsies) and by clinical and/or radiological follow-up in the remaining 121/139 cases (87.1%). The average time of the follow-up was 5 years and 6 months.

► **Table 2** Diagnosis of focal splenic incidentalomas in all study patients.

Benign FSI	Number (%) of patients	Malignant FSI	Number (%) of patients
Indeterminate benign masses	119 (91.5)	Malignant splenic lymphoma *	7 (77.8)
Splenoma (splenic hamartoma) *	3 (2.3)	Melanoma metastasis *	1 (11.1)
Granulomatous inflammation *	2 (1.6)	Chloroma in AML *	1 (11.1)
Non-specific inflammatory reaction *	1 (0.8)	–	–
Hemangioma *	1 (0.8)	–	–
Normal spleen tissue *	1 (0.8)	–	–
Splenic cyst *	1 (0.8)	–	–
Extramedullary hematopoiesis *	1 (0.8)	–	–
Littoral cell angioma *	1 (0.8)	–	–
Total number of patients with benign FSI	130 (100)	Total number of patients with malignant FSI	9 (100)

AML: acute myeloid leukemia; FSI: focal splenic incidentaloma. \*The diagnosis was confirmed histologically.

In 7/9 malignant cases (77.8%) the diagnosis of an mFSI was confirmed by histologic examination of the FSI. In the other 2 cases (22.2%), the diagnosis was confirmed by a histologic examination of a distant malignant lesion and by complete regression of FSI under chemotherapy. Of 130 bFSIs, the diagnosis was confirmed based on histologic examination in 11/130 cases (8.5%) and on clinical and radiological follow-up in 122/130 cases (91.5%). The final diagnoses of FSI in all the patients are shown in ► **Table 2**.

### Classification of splenic incidentalomas based on medical history

In total, 97/139 patients (69.8%) had splenic incidentalomas in a strict sense. In this group, 91/97 lesions (93.8%) were benign and 6/97 lesions (6.2%) were malignant. The malignant lesions were nodular splenic lymphomas in all patients.

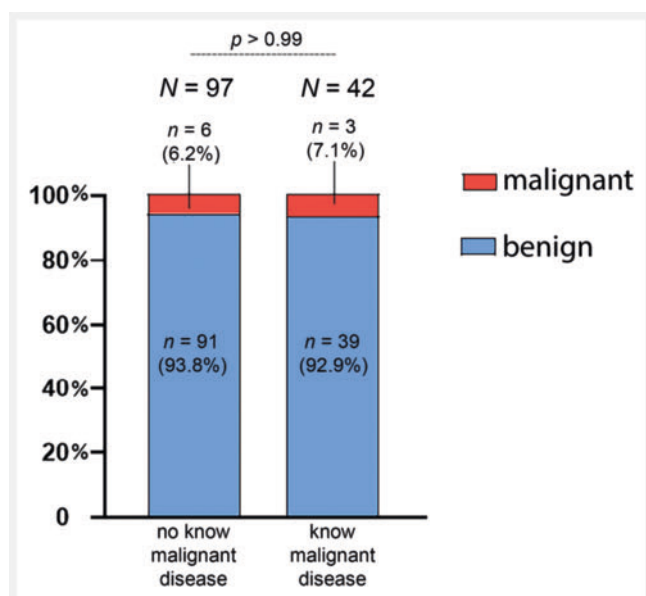
In addition, 42/139 patients (30.2%) had splenic incidentalomas in an extended sense, with known malignant disease in their medical history (24 cases with a current and 18 cases with a prior history of malignant underlying disease). In this group, 39/42 lesions (92.2%) were benign and 3/42 lesions (7.1%) were malignant. In patients with a current malignant underlying disease, 2/24 lesions (8.3%) were malignant, and, in patients with a prior history of malignant underlying disease, 1/18 lesions (5.6%) were malignant.

The malignant lesions were one melanoma metastasis in a patient with prior history of malignant melanoma, one lymphoma in a patient with known lymphoma, and one chloroma in a patient with known acute myeloid leukemia (AML).

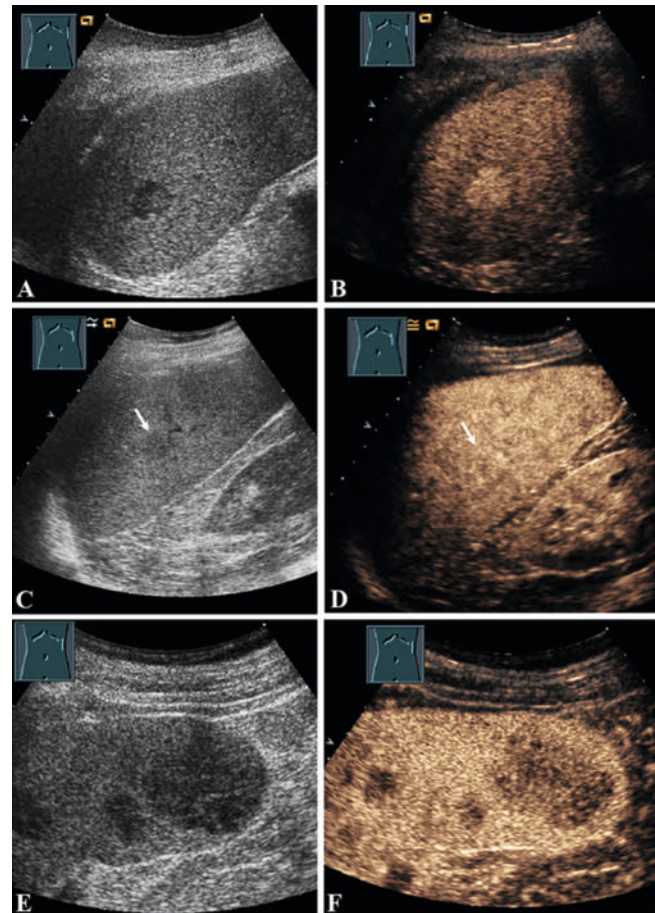
Of these 42 patients with FSI in an extended sense, 30/42 cases (71.4%) had a non-hematologic underlying malignancy (23 carcinomas, 2 germ cell tumors, 4 malignant melanomas, 1 malignant melanoma and carcinoma), 9/42 cases (21.4%) had a hematologic

underlying malignancy (6 malignant lymphomas, 3 cases of acute myeloid leukemia), and 3/42 cases (7.1%) had both a non-hematologic and a hematologic underlying malignancy (3 malignant lymphomas and carcinomas).

The frequency of mFSI was not significantly different in patients with a known malignant disease compared with those without a known malignant disease ( $p > 0.99$ , Fisher's exact test; ► **Fig. 1**).



► **Fig. 1** Malignancy rate of N = 139 splenic incidentalomas according to the presence of an underlying malignant disease in the medical history of study patients.



► **Fig. 2** Group 1: (A) A 71-year-old male patient with an incidentally detected hypoechoic splenic lesion on B-mode ultrasound and without a history of malignancy. (B) On contrast-enhanced ultrasound, the lesion showed arterial hyperenhancement after 60 s. A clinical follow-up of 5 years and 3 months revealed no evidence of malignancy. The diagnosis of an indeterminate benign mass was made. (C) A 63-year-old male patient with an incidentally detected hypoechoic splenic lesion on B-mode ultrasound (arrow) and without a history of malignancy. (D) On contrast-enhanced ultrasound, the lesion showed an arterial iso-enhancement after 27 s (arrow). The histopathologic examination of an enlarged mesenteric lesion revealed the diagnosis of Hodgkin's lymphoma. In the follow-up ultrasound after rituximab therapy, the lesion was no longer detectable. The diagnosis of splenic involvement in Hodgkin's disease was made. (E) A 63-year-old male patient with an incidentally detected hypoechoic splenic lesion on B-mode ultrasound, without a history of malignancy. (F) On contrast-enhanced ultrasound, the lesion showed arterial hypoenhancement after 37 s. A splenectomy was performed, and the diagnosis of primary splenic follicular lymphoma was confirmed histologically.

## Ultrasound examination

### B-mode ultrasound data

On B-US, 71/139 FSIs (51.1%) were hypoechoic (group I) (▶ Fig. 2), 58/139 (41.7%) were hyperechoic (group II) (▶ Fig. 3), and 10/139 (7.2%) were echogenic or cystic/complex (group III), 7 of which were echogenic cystic and 3 had a complex echogenicity (▶ Fig. 4).

Of the malignant lesions, 6/9 cases (66.6%) were hypoechoic (▶ Fig. 2C–D and E–F) and 3/9 (33.3%) cases hyperechoic on B-US (▶ Fig. 3C–D).

Further detailed diagnostic data from the B-US examination are summarized in ▶ Table 3.

### Contrast-enhanced ultrasound data

Regarding AE, 44/139 cases (31.7%) showed arterial hyperenhancement (▶ Fig. 2B and ▶ Fig. 3B), 18/139 cases (12.9%) arterial isoenhancement (▶ Fig. 2D), 67/139 cases (48.2%) arterial hypoenhancement (▶ Fig. 2F), and 10/139 cases (7.2%) absent arterial enhancement (▶ Fig. 4B and D). Of 9 mFSIs, 8/9 cases

(88.9%) showed hypoenhancement and 1/9 cases (11.1%) isoenhancement.

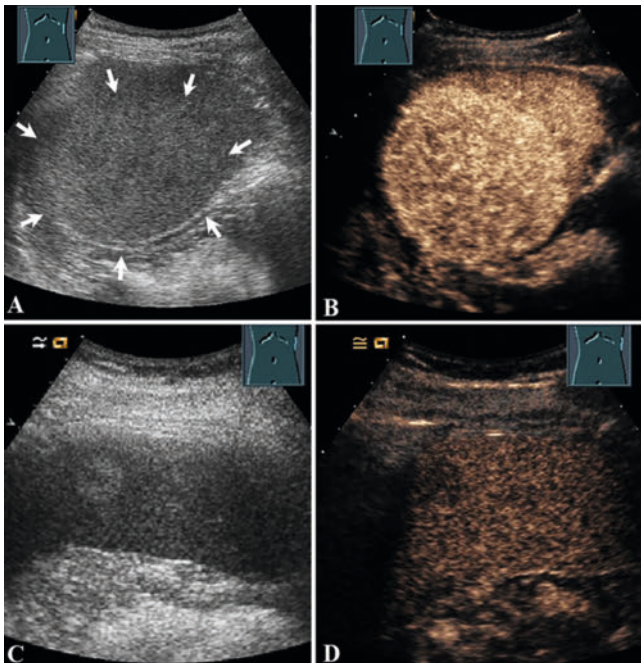
Regarding echogenicity in 5/139 cases (3.6%) and arterial enhancement in 7/139 cases (5.0%), there was a discrepancy between the first and second investigator, and the final decision was made by a third investigator. The agreement between the examiners for the ultrasound finding was “very good” (Cohen’s kappa = 0.9).

### Classification of splenic lesions based on B-mode ultrasound and contrast-enhanced ultrasound patterns

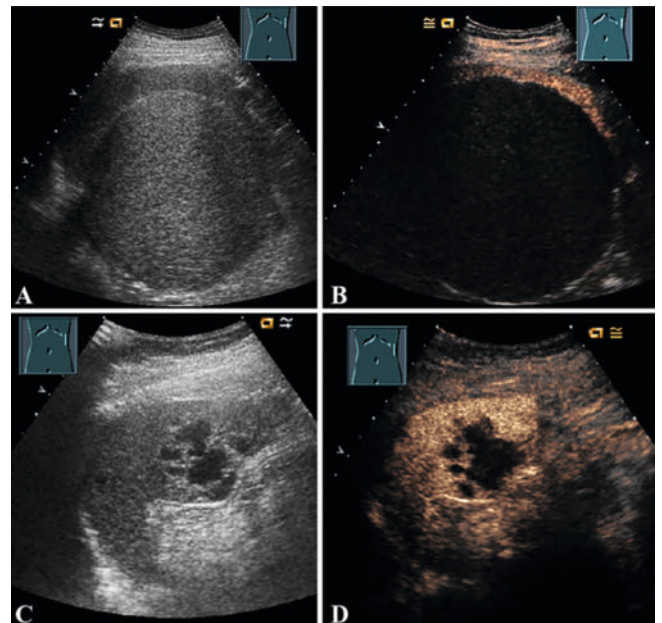
The number and malignancy rate of FSIs according to the modified classification of Bert and Görg et al. [11] is presented in ▶ Fig. 5.

## Discussion

Improved imaging techniques with high resolution and the increased use of additional imaging methods have led to an increase in incidental findings in different organs [15]. In the literature, the FSIs detected via imaging methods are described as rare, with a prevalence of less than 1% [16, 17]. In accordance with previous studies, the FSIs in this study were indeed rare and revealed a prevalence of 0.06%. Compared with previous studies, the smaller



▶ Fig. 3 Group 2: (A) A 54-year-old female patient with an incidentally detected hyperechoic splenic lesion on B-mode ultrasound (arrow), without a history of malignancy. (B) On contrast-enhanced ultrasound, the lesion showed arterial hyperenhancement after 9 s. A sonographic follow-up of 4 years and 6 months revealed no size progression. The diagnosis of an indeterminate benign mass was made. (C) A 56-year-old male patient with an incidentally detected hyperechoic splenic lesion on B-mode ultrasound and with known acute myeloid leukemia (AML). (D) On contrast-enhanced ultrasound, the lesion showed arterial hypoenhancement after 44 s. The patient died 1 year and 3 months later due to a cerebral manifestation of AML and massive cerebral hemorrhage. At autopsy, focal nodular blast infiltration (chloroma) of the spleen was histologically confirmed.

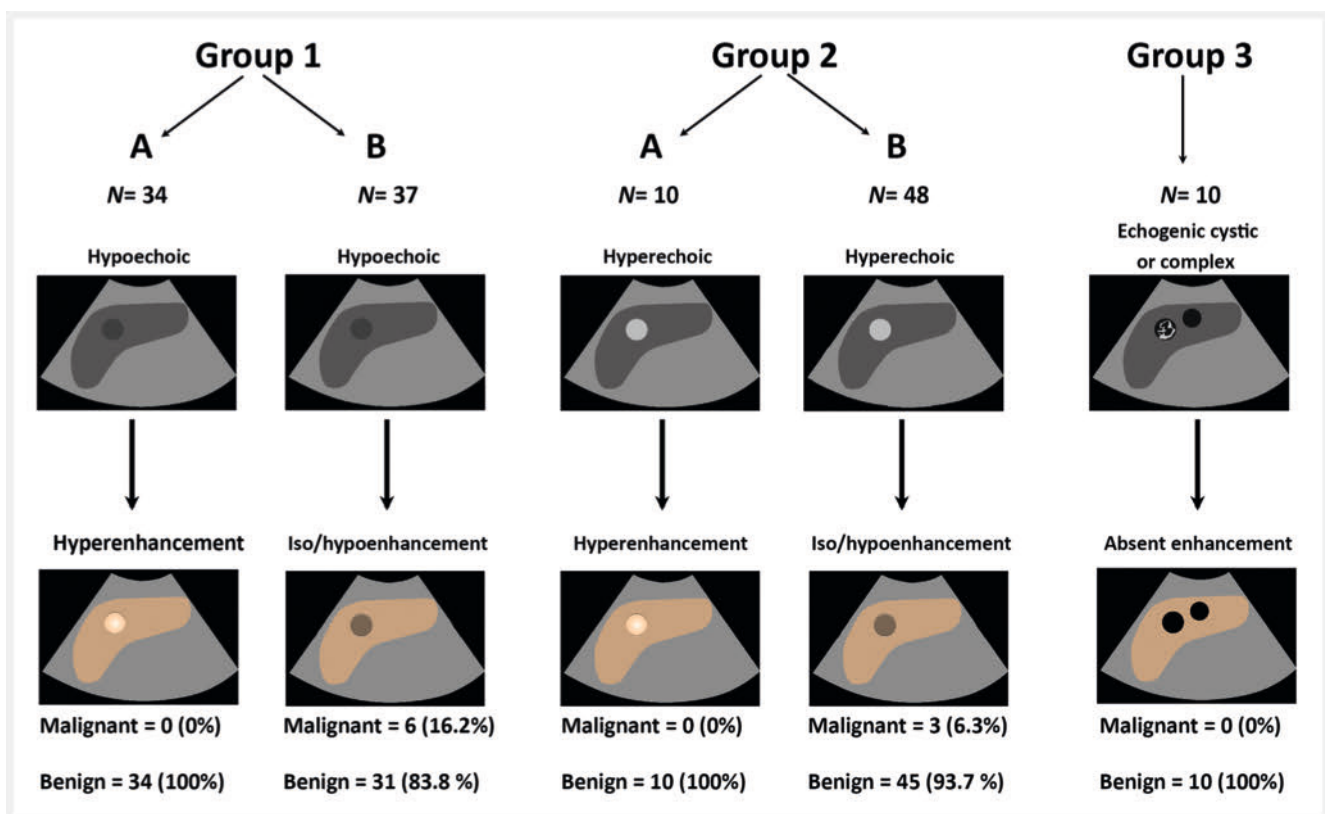


▶ Fig. 4 Group 3: (A) A 30-year-old male patient with an incidentally detected echogenic cystic splenic lesion on B-mode ultrasound, without a history of malignancy. (B) On contrast-enhanced ultrasound, the lesion showed absent enhancement during the whole investigation. A sonographic follow-up of 8 years and 4 months revealed no size progression. The diagnosis of an indeterminate benign mass was made. (C) A 45-year-old female patient with an incidentally detected complex lesion (cystic with solid parts) on B-mode ultrasound and prior known endometrial carcinoma. (D) On contrast-enhanced ultrasound, the lesion showed predominantly absent enhancement during the whole investigation. A sonographic follow-up of 3 years revealed no size progression. The diagnosis of an indeterminate benign mass was made.

► **Table 3** B-mode ultrasound data of the  $N = 139$  patients, subdivided between final malignant and benign focal splenic incidentalomas.

B-US feature	All FSIs $N = 139$	Malignant FSIs $n = 9$	Benign FSIs $n = 130$	$p$ -value
Hypoechoic	71 (51.1%)	6 (66.7%)	65 (50.0%)	0.49*
Not hypoechoic	68 (48.9%)	3 (33.3%)	65 (50.0%)	
Solitary lesion	84 (60.4%)	7 (77.8%)	77 (59.2%)	0.48*
Multiple lesions	55 (39.6%)	2 (22.2%)	53 (40.8%)	
Average size of lesions (cm)	2.6	3.8	2.6	0.17**

B-US: B-mode ultrasound; FSI: focal splenic incidentaloma unless otherwise noted, the values are indicated as number (%). A  $p$ -value of  $< 0.05$  was defined as significant. \*Fisher's exact test; \*\*Mann-Whitney test



► **Fig. 5** The number and malignancy rate of 139 FSIs in different groups according to the modified classification of Bert and Görg.

number of patients enrolled in the study during the long recruitment period may be due to differences in the definitions of the inclusion criteria [10, 18].

Overall, 6.5% of the FSIs were shown to be malignant, and 93.5% were benign. 6.2% of lesions were malignant in patients without a history of malignancy, and 7.1% of lesions in patients with a history of malignancy. Previous studies have shown a malignancy rate of 1–33.8% of splenic lesions in patients without a history of malignancy and 33.8–86.7% in patients with a history of malignancy [10, 18, 19]. This wide range of malignancy rates

in various studies may be caused by differences in patient spectra and in the definition criteria of splenic incidentalomas (► **Table 4**).

We observed no significantly different frequencies in malignancy of FSIs according to the presence or absence of a malignant disease in the medical history of the patients ( $p > 0.99$ , Fisher's exact test). Based on these findings, known malignant disease should not be considered as a highly determinant factor in the diagnostic workup of FSIs. This result is in line with previous studies, which showed that the spleen is an uncommon site for metastatic disease. A large autopsy study in 1898 patients with a solid malignant tumor showed that splenic metastasis was present in

► **Table 4** Malignancy rates of splenic lesions in patients with and without a history of malignancy.

Imaging modality	Cases	Year	Author	Patients with a history of malignancy (%)	Patients without a history of malignancy (%)	Study characteristics
US	136	2011	Stang et al. [10]	80.9	33.8	<ol style="list-style-type: none"> <li>1. The criteria for splenic incidentalomas were not defined</li> <li>2. Cysts, infarction, abscess, sarcoidosis, and diffuse micronodular infiltration by lymphoma were excluded from the study</li> </ol>
CT, MRI, and PET/CT	53	2013	Dhyani et al. [19]	86.7	2.6	<ol style="list-style-type: none"> <li>1. Only patients under the age of 30 years were included</li> <li>2. Lesions detected on staging examinations performed for evaluation of malignant disease were included in the study</li> <li>3. Splenic infarcts were included</li> </ol>
CT	379	2018	Siewert et al. [18]	33.8*	1.0	<ol style="list-style-type: none"> <li>1. Splenic infarcts and calcified granulomas were excluded</li> <li>2. Splenic cysts were included</li> <li>3. Splenic lesions in patients with known malignancy were not considered to be incidentalomas</li> <li>4. Only lesions in asymptomatic patients without history of malignancy were defined as incidentalomas</li> </ol>
US	139	2022	Present study	7.1	6.2	<ol style="list-style-type: none"> <li>1. Focal splenic incidentalomas were defined as asymptomatic and unexpected splenic lesions discovered incidentally on US, unrelated to the presenting illness</li> <li>2. Splenic infarcts and purely cystic anechoic lesions were excluded</li> </ol>

CT: computed tomography; MRI: magnetic resonance imaging; PET/CT: positron emission tomography/computed tomography; US: ultrasound; \*: these lesions were not defined as incidentalomas

only 3% of patients [20]. Furthermore, an ultrasound study in 680 patients with histologic evidence of malignant lymphoma detected splenic involvement in less than 15% of patients [21].

Regarding B-US patterns, EFSUMB guidelines describe small echogenic lesions as usually benign and hypoechoic lesions as more frequently malignant [7]. In this study, in accordance with EFSUMB statements, the majority of malignant lesions (66.7%) were hypoechoic and larger than benign lesions (3.6 cm vs 2.6 cm). However, in terms of B-US echo patterns, we found no significant difference between benign and malignant FSIs ( $p > 0.05$ ), which suggests non-specificity of B-US characteristics with respect to the malignancy of FSIs.

Regarding CEUS patterns, EFSUMB guidelines describe absent enhancement or arterial phase hyper-/isoenhancement as characteristic of benign lesions [7]. In accordance with EFSUMB statements, in the present study, all FSIs with absent enhancement or arterial hyperenhancement were benign. However, contrary to the EFSUMB guidelines, one lesion with arterial isoenhancement was shown to be a malignant lymphoma. These results are in accordance with findings from a previous study that demonstrat-

ed that 46.3% of splenic lymphomas show arterial isoenhancement [22]. Therefore, arterial isoenhancement should not be used as a predictor factor of benignity.

In the additional evaluation, we classified splenic incidentalomas using established B-US and CEUS criteria into five groups and subsequently followed them in terms of malignancy during their clinical course. The hypoechoic and hyperechoic lesions with arterial hyperenhancement (groups 1a and 2a) and the echogenic cystic or complex lesions with predominantly absent enhancement (group 3) were all benign. Furthermore, arterial iso-/hypoenhancement on CEUS may indicate FSI malignancy. However, the malignancy rate is different between hypoechoic and hyperechoic FSIs. In the present study, 16.2% of hypoechoic lesions with arterial hypo-/isoenhancement (group 1b) and 6.3% of hyperechoic lesions with arterial hypo-/isoenhancement (group 2b) were malignant. Based on these results, the lesions reveal different malignancy rates depending on the group, and this classification may be helpful in further evaluation of FSIs.

There are some limitations to this study. These include the general limitations of ultrasound examinations, which are charac-

terized by high interobserver and interequipment variability. Furthermore, the study was performed only in patients who were referred to the Interdisciplinary Center of Ultrasound Diagnostics for the investigation of abdominal pathologies. Therefore, selection bias cannot be excluded. Histologic confirmation was not performed in all patients with an FSI. However, all diagnoses in these patients were verified by clinical and/or radiological follow-up. Another limitation of our study is the semiquantitative classification of the ultrasound data, which may lead to more scope for interpretation than a quantitative method. However, the inter-rater observer variability for the ultrasound findings demonstrated “very good” agreement. Due to the retrospective nature of the study and the relatively small number of subjects ( $N = 139$ ), further prospective multicentric studies are needed to validate our findings.

## Conclusion

In summary, classification according to the B-US and CEUS patterns may be useful in evaluating the malignancy of FSIs. In all patients with a hypoechoic or hyperechoic lesion with arterial hypo-/isoenhancement, further imaging and short-term imaging follow-up or histologic confirmation are indicated even if the patient has no history of a malignant disease. In patients with a hypoechoic or hyperechoic lesion with arterial hyperenhancement and in those with an echogenic cystic or complex lesion with predominantly absent enhancement, only imaging follow-up should be performed.

## Conflict of Interest

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

## References

- [1] Krumbhaar EB. FUNCTIONS OF THE SPLEEN: (Mysterii Plenum Organon) Galen. *Physiological Reviews* 1926; 6: 160–200. doi:10.1152/physrev.1926.6.1.160
- [2] Görg C. The forgotten organ: contrast enhanced sonography of the spleen. *Eur J Radiol* 2007; 64: 189–201. doi:10.1016/j.ejrad.2007.06.036
- [3] Caremani M, Occhini U, Caremani A et al. Focal splenic lesions: US findings. *Journal of ultrasound* 2013; 16: 65–74. doi:10.1007/s40477-013-0014-0
- [4] Barat M, Hoeffel C, Aissaoui M et al. Focal splenic lesions: Imaging spectrum of diseases on CT, MRI and PET/CT. *Diagn Interv Imaging* 2021; 102: 501–513. doi:10.1016/j.diii.2021.03.006
- [5] Dietrich CF, Nolsøe CP, Barr RG et al. 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. *Ultraschall in Med* 2020; 41: 562–585. doi:10.1055/a-1177-0530
- [6] Trenker C, Görg C, Freeman S et al. WFUMB Position Paper-Incidental Findings, How to Manage: Spleen. *Ultrasound Med Biol* 2021; 47: 2017–2032. doi:10.1016/j.ultrasmedbio.2021.03.032
- [7] Sidhu P, Cantisani V, Dietrich C et al. The EFSUMB Guidelines and Recommendations for the Clinical Practice of Contrast-Enhanced Ultrasound (CEUS) in Non-Hepatic Applications: Update 2017 (Long Version). *Ultraschall in Med* 2018; 39: e2–e44. doi:10.1055/a-0586-1107
- [8] Heese F, Görg C. Diagnostische Wertigkeit einer internistischen Referenzsonographie (DEGUM-Stufe 3). *Ultraschall in Med* 2006; 27: 220–224. doi:10.1055/s-2006-926665
- [9] Görg C, Graef C, Bert T. Contrast-enhanced sonography for differential diagnosis of an inhomogeneous spleen of unknown cause in patients with pain in the left upper quadrant. *J Ultrasound Med* 2006; 25: 729–734. doi:10.7863/jum.2006.25.6.729
- [10] Stang A, Keles H, Hentschke S et al. Incidentally detected splenic lesions in ultrasound: does contrast-enhanced ultrasonography improve the differentiation of benign hemangioma/hamartoma from malignant lesions? *Ultraschall Med* 2011; 32: 582–592. doi:10.1055/s-0031-1282034
- [11] Bert T, Tebbe J, Görg C. What Should be Done with Echoic Splenic Tumors Incidentally Found by Ultrasound? *Z Gastroenterol* 2010; 48: 465–471. doi:10.1055/s-0028-1109784
- [12] Goerg C, Schwerek WB, Goerg K. Splenic lesions: sonographic patterns, follow-up, differential diagnosis. *European Journal of Radiology* 1991; 13: 59–66. doi:10.1016/0720-048X(91)90058-4
- [13] Neesse A, Huth J, Kunsch S et al. Contrast-enhanced ultrasound pattern of splenic metastases – a retrospective study in 32 patients. *Ultraschall in Med* 2010; 31: 264–269. doi:10.1055/s-0028-1109812
- [14] Lim AKP, Patel N, Eckersley RJ et al. Evidence for Spleen-specific Uptake of a Microbubble Contrast Agent: A Quantitative Study in Healthy Volunteers. *Radiology* 2004; 231: 785–788. doi:10.1148/radiol.2313030544
- [15] O’Sullivan JW, Muntinga T, Grigg S et al. Prevalence and outcomes of incidental imaging findings: umbrella review. *BMJ* 2018; 361: k2387. doi:10.1136/bmj.k2387
- [16] James MK, Francois MP, Yoeli G et al. Incidental findings in blunt trauma patients: prevalence, follow-up documentation, and risk factors. *Emergency Radiology* 2017; 24: 347–353. doi:10.1007/s10140-017-1479-5
- [17] Schölmerich J, Lüttgens A, Volk BA et al. Unexpected findings during abdominal sonography. Their incidence and clinical significance. *Dtsch Med Wochenschr* 1986; 111: 807–811. doi:10.1055/s-2008-1068535
- [18] Siewert B, Millo NZ, Sahi K et al. The Incidental Splenic Mass at CT: Does It Need Further Work-up? An Observational Study. *Radiology* 2018; 287: 156–166. doi:10.1148/radiol.2017170293
- [19] Dhyani M, Anupindi SA, Ayyala R et al. Defining an imaging algorithm for noncystic splenic lesions identified in young patients. *AJR Am J Roentgenol* 2013; 201: W893–899. doi:10.2214/ajr.12.10105
- [20] Schön CA, Görg C, Ramaswamy A et al. Splenic metastases in a large unselected autopsy series. *Pathology – Research and Practice* 2006; 202: 351–356. doi:10.1016/j.prp.2005.12.008
- [21] Görg C, Weide R, Schwerek WB. Malignant splenic lymphoma: sonographic patterns, diagnosis and follow-up. *Clin Radiol* 1997; 52: 535–540. doi:10.1016/s0009-9260(97)80331-5
- [22] Görg C, Faoro C, Bert T et al. Contrast enhanced ultrasound of splenic lymphoma involvement. *Eur J Radiol* 2011; 80: 169–174. doi:10.1016/j.ejrad.2009.11.012