

# Common pitfalls when using the Liver Imaging Reporting and Data System (LI-RADS): lessons learned from a multi-year experience

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## Abstract

The goal of the Liver Imaging Reporting and Data System (LI-RADS) is to standardize the interpretation and reporting of liver observations on contrast-enhanced CT and MR imaging of patients at risk for hepatocellular carcinoma. Although LI-RADS represents a significant achievement in standardization of the diagnosis and management of cirrhotic patients, complexity and caveats to the algorithm may challenge correct application in clinical practice. The purpose of this paper is to discuss common pitfalls and potential solutions when applying LI-RADS in practice. Knowledge of the most common pitfalls may improve the diagnostic confidence and performance when using the LI-RADS system for the interpretation of CT and MR imaging of the liver.

**Key words:** Hepatocellular carcinoma—Multidetector computed tomography—Magnetic resonance imaging

The Liver Imaging Reporting and Data System (LI-RADS), supported by the American College of Radiology (ACR), represents the culmination of years of dynamic development informed by emerging evidence, user feedback, and ultimately expert consensus. LI-RADS consists of four major imaging algorithms applied to different contexts: (1) US LI-RADS for screening and surveillance, (2) CT/MRI Diagnostic LI-RADS for staging and diagnosis, (3) CEUS LI-RADS for diagnosis, and (4) CT/MRI Treatment Response algorithm for assessing response to locoregional therapies. The newest version 2018 heralds a

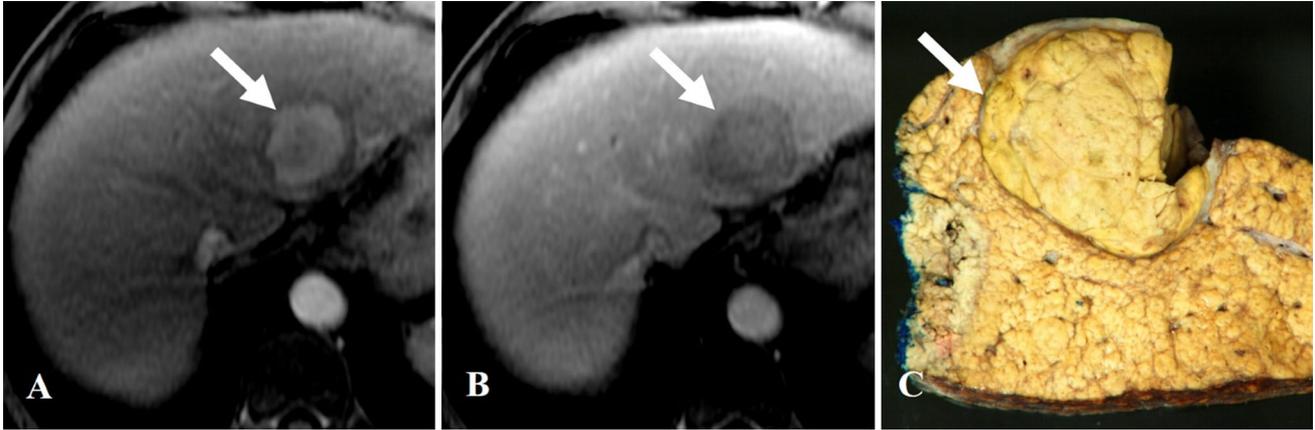
major milestone with the unification of LI-RADS criteria within the American Association for the Study of Liver Diseases (AASLD) guidelines [1, 2]. LI-RADS diagnostic algorithms follow a stepwise approach to categorize each liver observation according to the risk of being hepatocellular carcinoma (HCC), as follows: LR-1 (Definitely benign), LR-2 (Probably benign), LR-3 (Intermediate probability of malignancy), LR-4 (Probably HCC), and LR-5 (Definitely HCC) [3]. In addition to stratifying HCC probability, other key distinctions include differentiation of HCC from non-HCC malignancies and distinction of malignancies with tumor in vein (TIV) from those without.

Liver imaging is by no means a simple task, and the necessary complexity of the algorithm and the large number of imaging features may complicate the use of the system in clinical practice. With the use of LI-RADS for multiple years at multiple institutions, we have noticed a few recurrent pitfalls that lead to a misuse of LI-RADS, thus reducing its diagnostic value.

In this manuscript we report five common pitfalls when using the LI-RADS system for the interpretation of contrast-enhanced CT and MRI studies in patients at risk for hepatocellular carcinoma. For each pitfall, a solution is proposed using the recommendations of LI-RADS v2018.

## Pitfall I: Applying LI-RADS in patients not at increased risk for hepatocellular carcinoma

LI-RADS diagnostic algorithm requires a high pre-test probability of HCC to achieve the desired specificity that allows for a definitive imaging diagnosis of HCC. Hence, the algorithm must be applied to a population that is



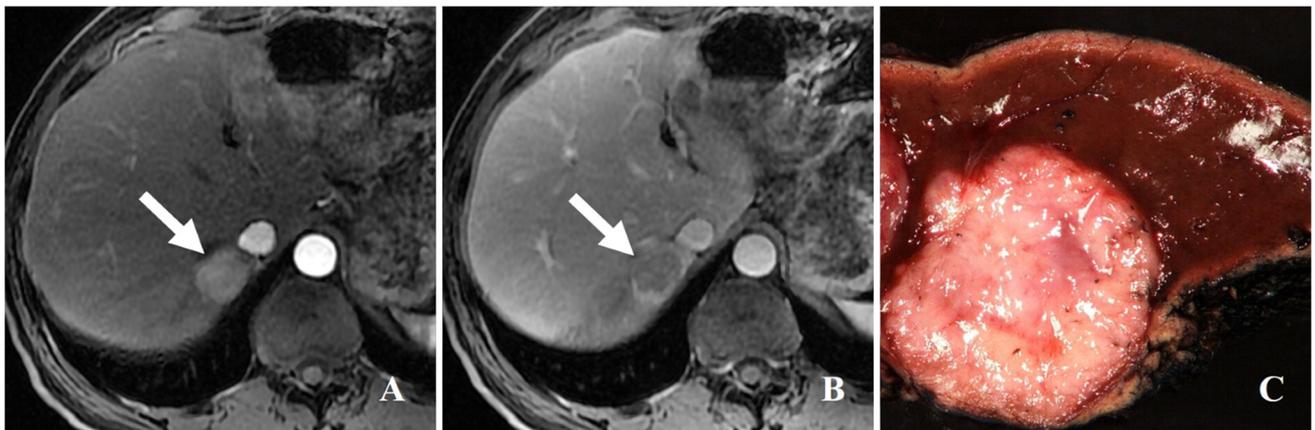
**Fig. 1.** 66-year-old man with HBV-related cirrhosis. Axial 3D-GRE gadobenate-MRI images obtained during the hepatic arterial phase (HAP) (a) and portal venous phase (PVP) (b) show a 4.0 cm LR-5 observation showing non-rim arterial

phase hyperenhancement (arrow, a) and “washout” (arrow, b). Gross pathology specimen from left hepatic resection confirms a well differentiated HCC (arrow, c).

sufficiently ‘at risk’. The optimal level of risk balanced against the cost-effectiveness of screening/surveillance is defined by the AASLD practice guidelines as HCC incidence > 1.5%/year [1, 4]. LI-RADS v2018 defines the at risk population as cirrhotic patients, patients with chronic hepatitis B even without cirrhosis, and patients with current or prior history of HCC [4]. When applied to a high-risk population, the intended specificity and positive predictive value for LR-5 diagnosis are on the order of 95% or higher. LI-RADS diagnostic table defines several scenarios that meet LR-5 criteria, all of which require a size of at least 10 mm and presence of non-rim arterial phase hyperenhancement (APHE) along with other major features of threshold growth (TG),

“washout”, and delayed-enhancing “capsule” appearance [2, 5] (Fig. 1).

In populations without sufficient pre-test probability (i.e., non cirrhotic patients or cirrhosis due to congenital hepatic fibrosis or vascular disorders), the LR-5 criteria do not carry the same diagnostic specificity. The combination of arterial phase hyperenhancement and “washout” can be seen in benign neoplasms and non-HCC malignancies, such as in hepatocellular adenoma (ranging from 5 to 8% of inflammatory to 70 to 100% of HNF1 $\alpha$ -mutated hepatocellular adenomas) [6, 7] and hypervascular metastases (e.g., from breast cancer, neuroendocrine tumor, renal cell carcinoma, melanoma, thyroid carcinoma) [8, 9] (Fig. 2). In cirrhosis secondary



**Fig. 2.** 68-year-old male with no history of chronic hepatic disease. MRI with gadoxetate disodium shows a 3.1 cm observation (arrows) with arterial phase hyperenhancement (APHE) on HAP (a), “washout” and enhancing “capsule” on PVP (b). The combination of imaging features applying the

LI-RADS algorithm would be compatible with LR-5. However, the LI-RADS system should not be used in this case because of lack of cirrhosis. Resection (c) revealed a metastasis from a previously unknown pancreatic neuroendocrine tumor.

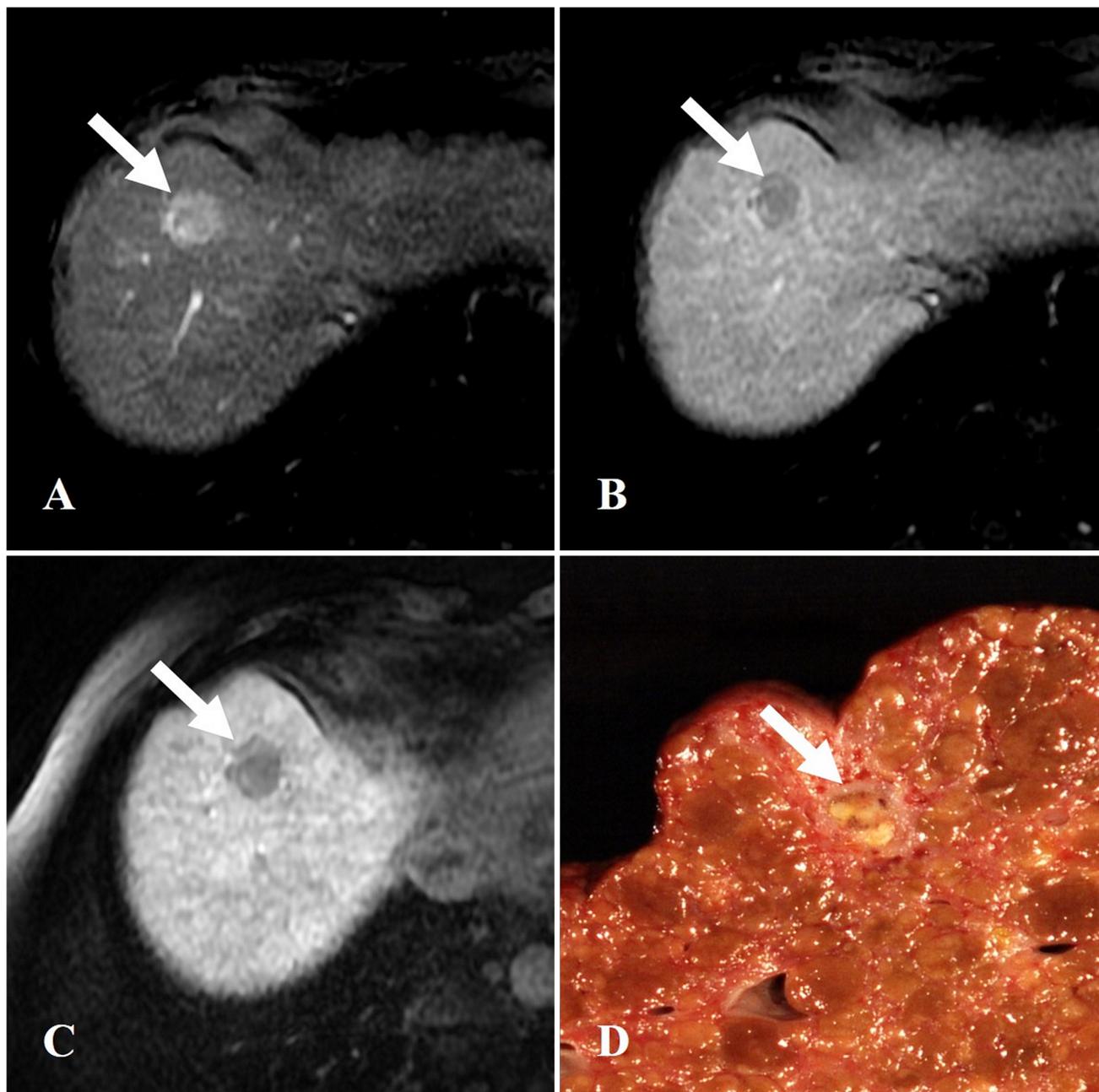


Fig. 3. 69-year-old female with history of NASH cirrhosis. On gadoxetate-MRI there is a 2.2 cm APHE observation on HAP (a) with “washout” on PVP (b) and hypointensity on HBP

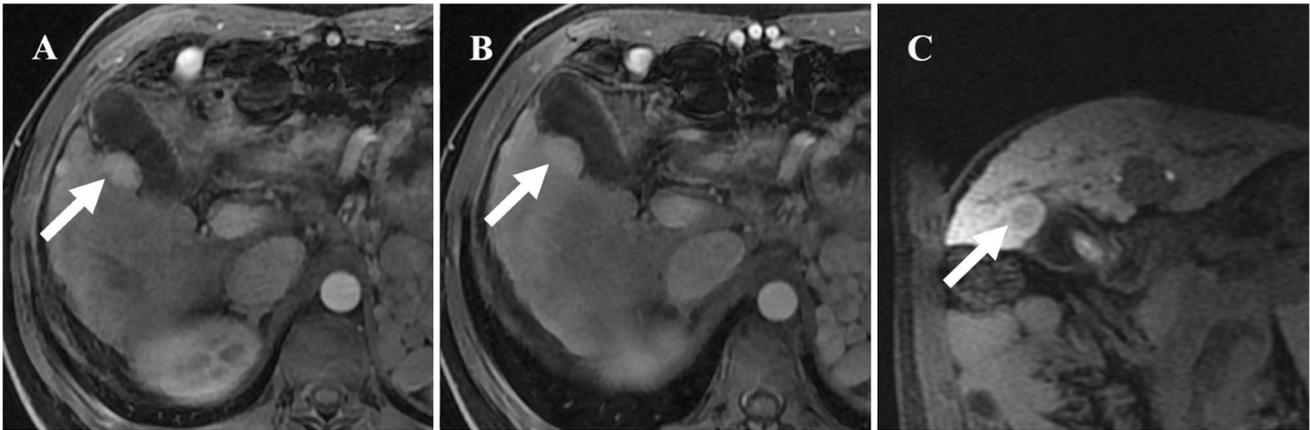
(c) consistent with a LR-5 observation. Pathological examination (d) after explant confirms a HCC.

to vascular disorders, large regenerative nodules may present as arterial hyperenhancing lesions, thus potentially mimicking HCC [10, 11].

*Solution* To maintain a high specificity for the diagnosis of HCC, the LI-RADS system should be applied only to a high-risk population. In other populations, multi-disciplinary discussion is recommended and it may be necessary to obtain a tissue biopsy for definitive diagnosis.

### Pitfall II: Interpreting hypointensity on transitional-hepatobiliary phase MR images as “washout” appearance

The “washout” appearance is defined as temporal reduction in enhancement of an observation resulting in unequivocal hypointensity compared to the surrounding liver parenchyma on the extracellular contrast phases [2,



**Fig. 4.** 41-year-old male with cirrhosis secondary to autoimmune hepatitis. Gadoxetate-MRI shows a 2.0 cm APHE observation on HAP (arrow, **a**) without evidence of

definitive “washout” on PVP (arrow, **b**) which appears hypointense on HBP (arrow, **c**). The lesion is a biopsy-proven regenerative nodule.



**Fig. 5.** 77-year-old man with history of HCV cirrhosis. Gadobenate-MRI demonstrates a 3.5 cm observation with non-rim APHE on HAP (**a**), “washout” and enhancing

“capsule” on PVP (arrow, **b**) and DP (arrow, **c**). This observation can be characterized as LR-5 (Definitely HCC).

[12]. The extracellular phases include the portal venous (PVP, 70–90 s) and delayed (DP, 3–5 min) phases when using an extracellular or a predominately extracellular agent, such as Gd-BOPTA (Gadobenate Dimeglumine). When using the hepatobiliary contrast agent Gd-EOB-DTPA (Gadoxetate Disodium), the extracellular phase of contrast is much shorter and refers only to the PVP [12]. Due to rapid uptake of gadoxetate by the hepatocytes, concurrent clearance of contrast from the vascular structures, and excretion into the biliary system, there is a more complex kinetic model and distribution of contrast following the portal venous phase. The interval time between the portal venous and hepatobiliary phase (HBP) is referred to as the transitional phase (TP) and occurs between 2 and 5 min after the injection of gadoxetate disodium. The characteristic imaging features of the transitional phase are progressive enhancement of the background liver which may initially equilibrate to and then become brighter than the blood pool contrast.

Hypointensity of an observation on TP images may be related to the uptake of contrast agent by the liver along with lack of uptake within the lesion, rather than true dynamic “washout” related to the vascularity of the mass [13] (Fig. 3).

“Washout” as defined on extracellular agent imaging, is a highly specific (reported range for specificity: 88–100%) imaging feature for the diagnosis of HCC in cirrhosis and is considered a major feature in LI-RADS system [5]. The expansion of interpretation of “washout” on TP and HBP images, while increasing the sensitivity (from 70.9% for PVP only “washout” to 93.8% for hypointensity on TP and HBP), also decreases the specificity for the diagnosis of HCC (from 97.7% of “washout” alone on PVP to 48.8% including the TP and HBP hypointensity) [14]. Hence, LI-RADS defines TP and HBP hypointensity as ancillary features favoring malignancy, not specific for HCC. This distinction is made to preserve specificity in the context of transplan-

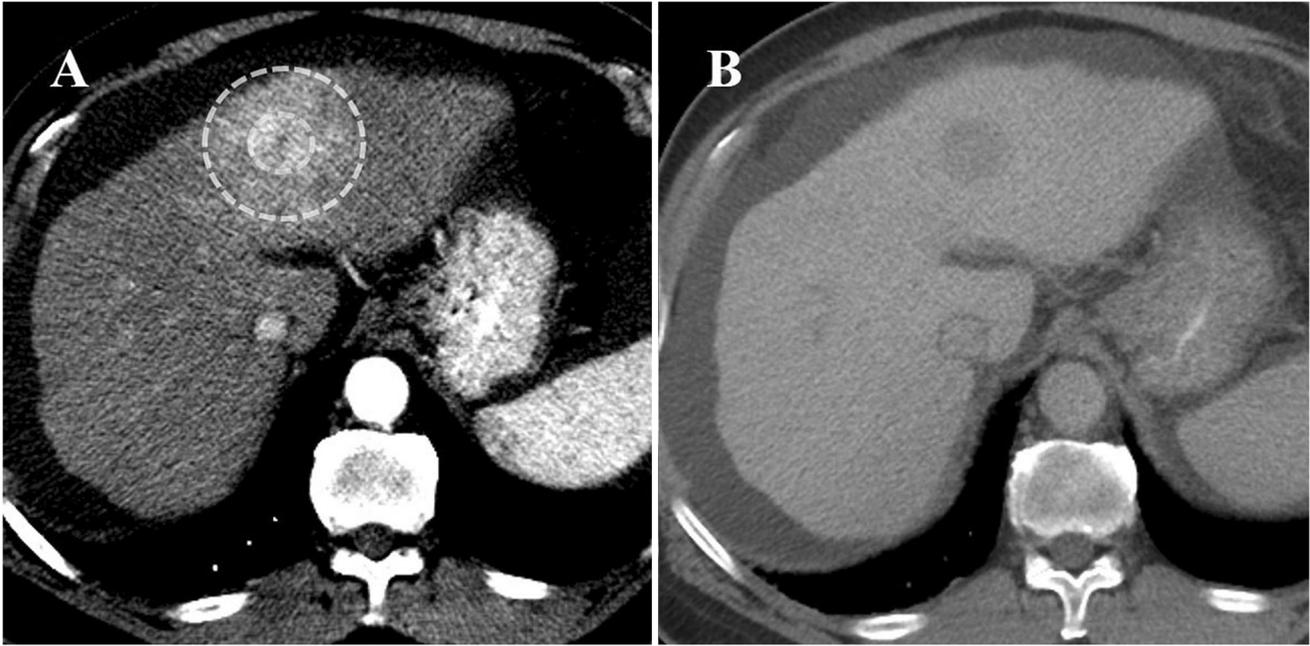


Fig. 6. Contrast-enhanced CT shows the presence of a APHE observation on HAP (a) surrounded by corona enhancement (between the inner and outer circles). This

type of enhancement should not be interpreted as an enhancing “capsule” appearance. Note that the perilesional enhancement is ill-defined and fades on the PVP image (b).

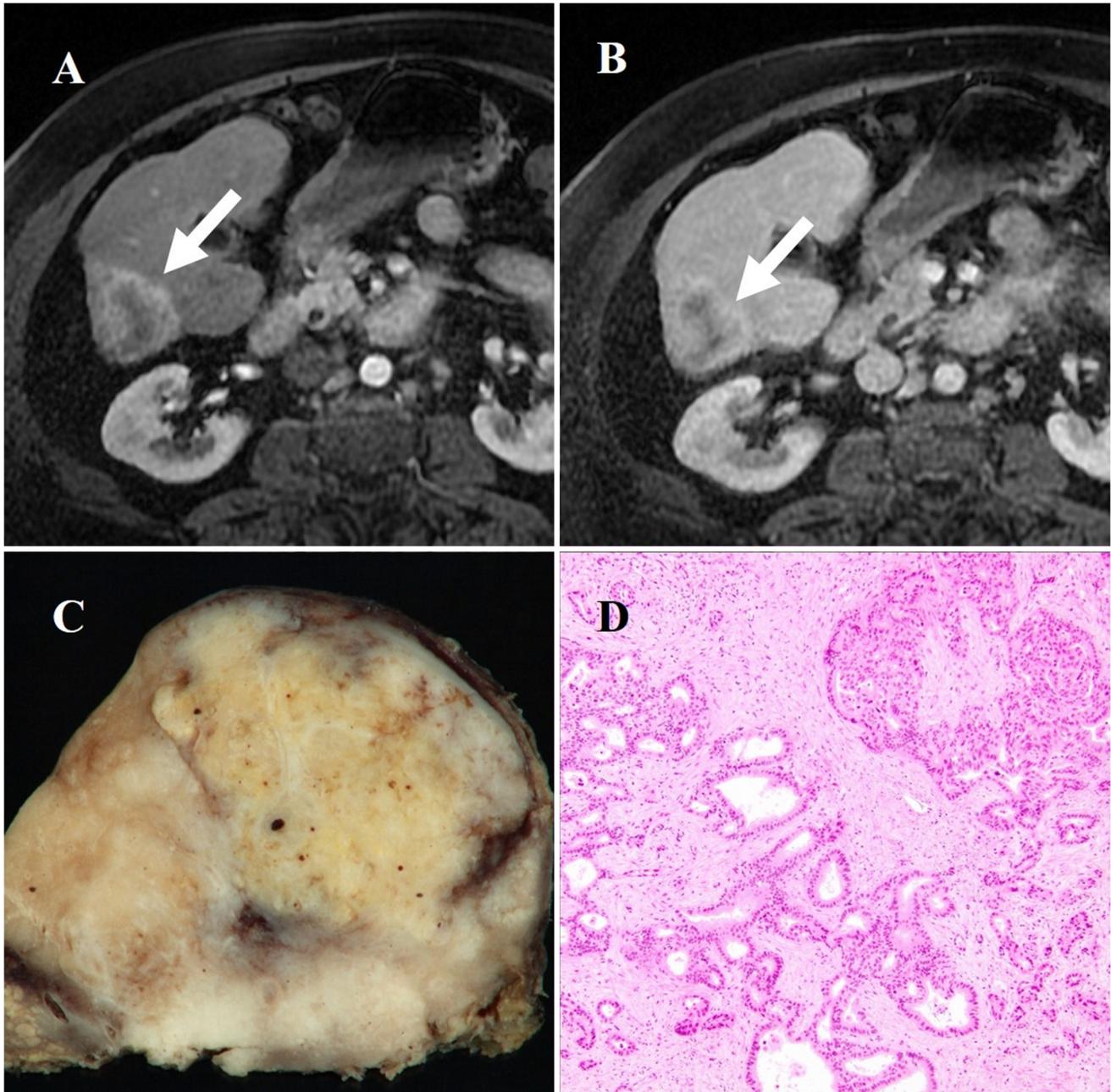
tation. Other entities in a cirrhotic liver that have been reported to present with APHE and hypointensity on HBP include small vascular shunts, flash-filling hemangiomas [15], small cholangiocarcinomas [16], mass-like confluent fibrosis [17], or dysplastic/regenerative nodules (Fig. 4).

**Solution** When MRI is performed with Gd-EOB-DTPA, the presence of “washout” should be assessed only on the images acquired during PVP. Future evidence may help to redefine the role of TP and HBP hypointensity, as these do serve as major features of HCC in other international guidelines, where the relative importance of resection over transplantation favors sensitivity over specificity [18, 19].

### Pitfall III: Interpreting any/all peri-observation enhancement as “capsule”

In LI-RADS, enhancing “capsule” appearance is a major feature for the diagnosis of HCC and is defined as a thin rim of perilesional hyperenhancement appreciated on the post-contrast images acquired during the portal venous or delayed phases [2, 12] (Fig. 5). The enhancing “capsule” has a reported sensitivity of 42–64% and specificity of 86–96% for the diagnosis of HCC [5]. The

inter-reader agreement for this major feature is lower than for APHE and washout, which may imply potential confusion regarding its application [20]. The enhancing “capsule” should be distinguished from other types of peripheral enhancement that can occur in liver observations including: surrounding delayed-enhancing fibrous septa/tissue, corona enhancement, rim APHE, and rim uptake on HBP. These different types of peripheral enhancement can be distinguished by scrutinizing the appearance and conspicuity on the post-contrast dynamic study. A “capsule” by definition should be thicker and/or more distinct than the surrounding fibrous septa and may encircle a nodule in whole or in part. Compressed adjacent fibrotic liver and fibrous septa can be difficult to distinguish from “capsule”. Corona enhancement is an ancillary feature favoring malignancy thought to be due to the peri-sinusoidal venous drainage occurring in the periphery of progressed HCC [21]. It appears as an ill-defined, irregular area of perilesional enhancement on HAP images fading on PVP and DP images [22, 23] (Fig. 6). Although rim APHE can be seen in atypical hepatocellular carcinoma, it is a sign concerning for a non-HCC malignancy (this feature will be further explored in Pitfall IV) (Fig. 7). Finally, a rim of contrast uptake on HBP images obtained after the injection of Gd-EOB-DTPA has been



**Fig. 7.** 63-year-old male with cirrhosis due to ethanol abuse. Gadoxetate-MRI demonstrates a 4.3 cm observation with rim APHE on HAP (arrow, **a**) and progressive central filling on PVP (arrow, **b**) classified as LR-M. Resection of the tumor (**c**) shows at macroscopic examination a firm well-

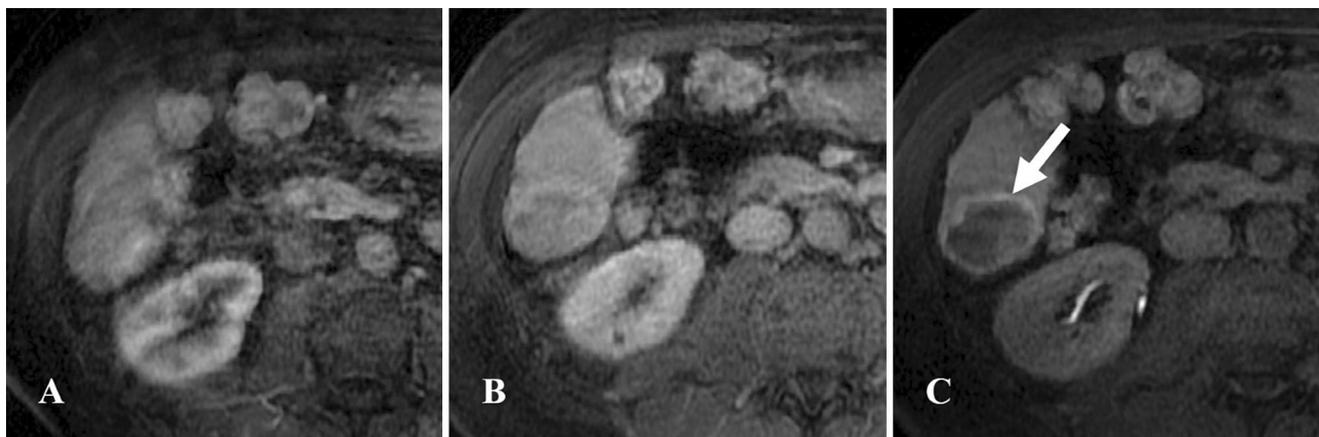
circumscribed white mass. Histopathological examination (**d**) shows a tumor with gland forming growth pattern, embedded in a desmoplastic stroma, confirming the diagnosis of an intra-hepatic cholangiocarcinoma.

reported in a small percentage (5.2% reported with a complete peripheral rim) of HCCs and correlated with hyperplastic hepatocytes at the periphery of the tumor [24] (Fig. 8).

*Solution* Carefully scrutinizing the appearance of peri-observational enhancement on the dynamic study permits a correct interpretation and use of the major feature, “capsule”.

#### **Pitfall IV: Not using the LR-M category**

The latest version of LI-RADS (v2018) defines the criteria to classify a liver observation as LR-M that is probably or definitely malignant but without the imaging features typical for HCC. These criteria include a “targetoid” mass or a non-targetoid mass presenting



**Fig. 8.** 65-year-old male with history of ethanol-related cirrhosis. Gadoxetate-MRI shows a heterogeneous APHE observation on HAP (a) with “washout” and enhancing “capsule” on PVP (b). The observation demonstrates also a

hyperintense rim (arrow) on HBP (c). Percutaneous needle biopsy confirmed the diagnosis of HCC (courtesy of Dr. Giuseppe Brancatelli, MD, University of Palermo, Palermo, Italy).

with an infiltrative appearance, marked diffusion restriction, necrosis, or severe ischemia. Targetoid appearance refers to a target-like dynamic contrast enhancement pattern characterized by rim APHE, peripheral “washout”, and central delayed enhancement [25]. A targetoid appearance can also be appreciated on the diffusion weighted imaging (DWI) and HBP. The appearance is thought to reflect peripheral hypercellularity and central stromal fibrosis or ischemia in the lesion [25]. This combination of imaging features suggests a non-HCC malignancy such as cholangiocarcinoma, combined hepatocellular carcinoma-cholangiocarcinoma [26] (Fig. 9), or metastasis (Fig. 10). The key distinction is often the differentiation of rim APHE from non-rim APHE and peripheral “washout” from non-peripheral “washout”.

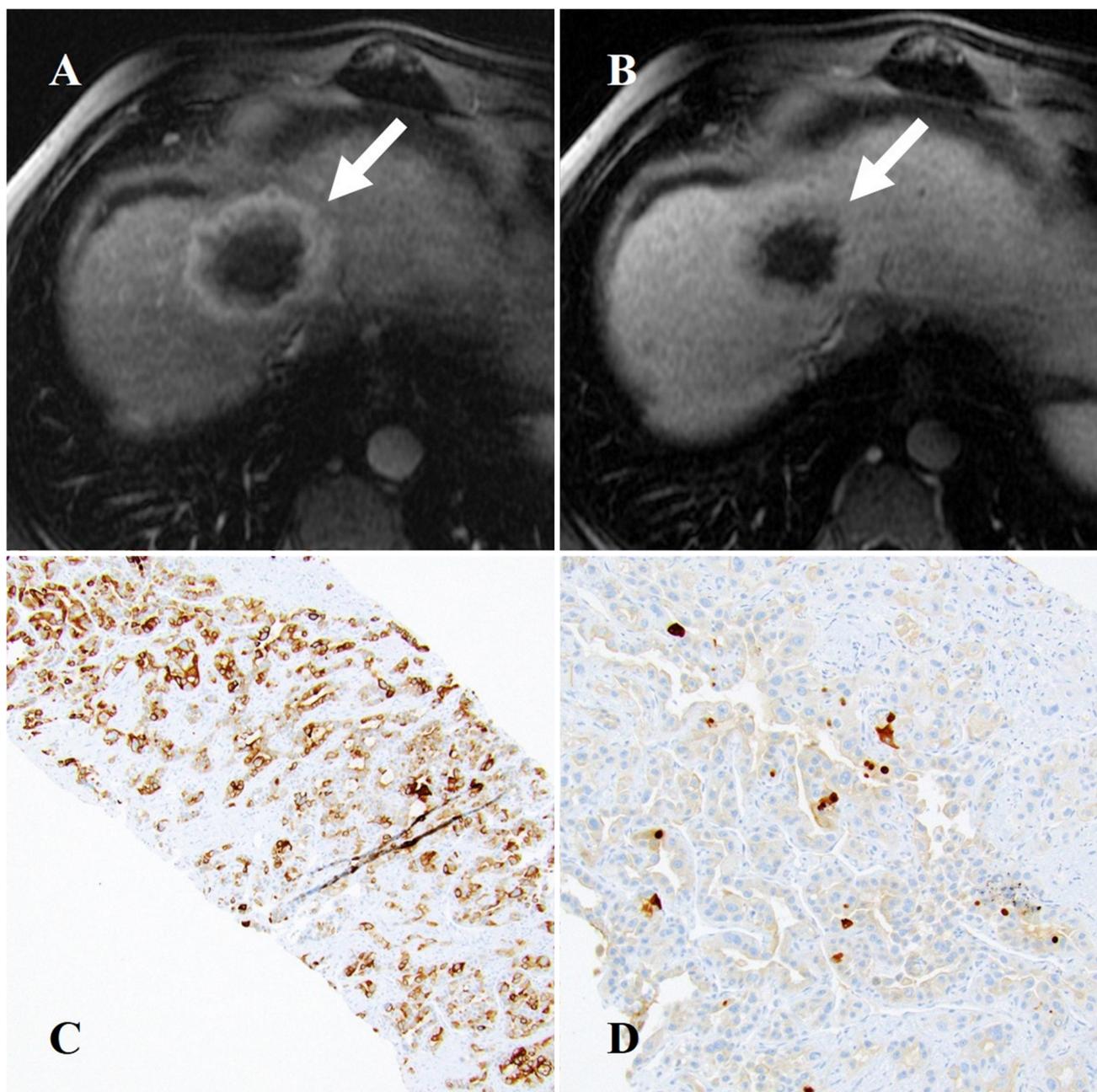
It is important to recognize the presence of these imaging features to place the observation in the LR-M category since the management implications are significantly different. A LR-M observation generally requires a discussion within a multi-disciplinary team and possibly a biopsy to confirm the non-HCC malignant nature that may affect patient’s eligibility for liver transplantation [27]. Of note, LR-M category does not exclude the diagnosis of HCC, since atypical HCC may present with a rim APHE [28].

**Solution** Rim APHE should not be misclassified as the major criterion non-rim APHE. A liver observation presenting with a targetoid appearance should be classified as LR-M.

### Pitfall V: Classifying any vascular thrombosis as tumor in vein

When interpreting a contrast-enhanced CT or MRI of a cirrhotic liver with a malignant lesion and vascular thrombosis, a potentially challenging task for the radiologist is to differentiate a bland venous thrombus from tumoral vascular invasion. In LI-RADS v2018 tumor in vein (TIV) is defined as enhancing soft tissue mass or thrombus within the portal or hepatic veins [2]. Not all venous thrombosis near a malignant observation should be classified as TIV and the diagnosis of TIV should only be made when unequivocal (Fig. 11). Findings suggesting the presence of tumor in vein rather than a bland thrombosis are the continuity of the thrombus with a malignant observation, expansion of the vessel [29] (Fig. 12) and restricted diffusion [30]. Of note, the presence of TIV is not necessarily diagnostic of HCC as it can also be seen in non-HCC malignancy (e.g., 34–48% of intra-hepatic cholangiocarcinoma) (Fig. 13) [31, 32]. LI-RADS v2017 version has introduced a categorization of the tumor in vein along with qualifying statements according to the probability of HCC ranging from LR-TIV “definitely due to HCC” when the tumor in vein is in continuity with a LR-5 observation to LR-TIV “may be due to non-HCC malignancy” in the presence of a targetoid mass.

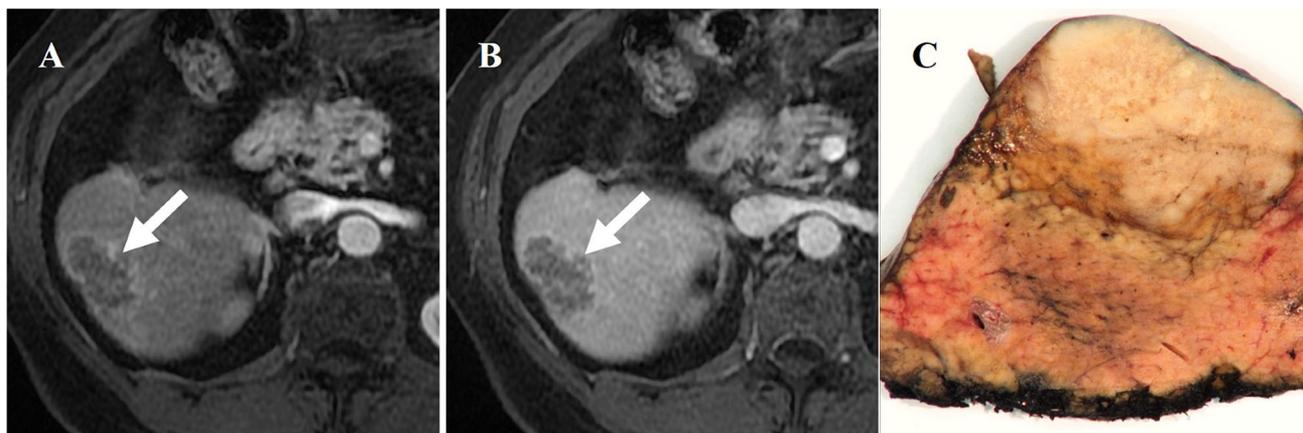
**Solution** Scrutiny of the morphologic appearance and enhancement of the thrombus is key to correctly assess TIV. TIV should only be applied when the features are unequivocal.



**Fig. 9.** 63-year-old male with cirrhosis due to ethanol abuse. Gadobenate-MRI shows a 6.8 cm targetoid observation with rim APHE on HAP (arrow, **a**) and progressive central enhancement on DP image (arrow, **b**). A percutaneous biopsy of the lesion was performed: immunohistochemistry

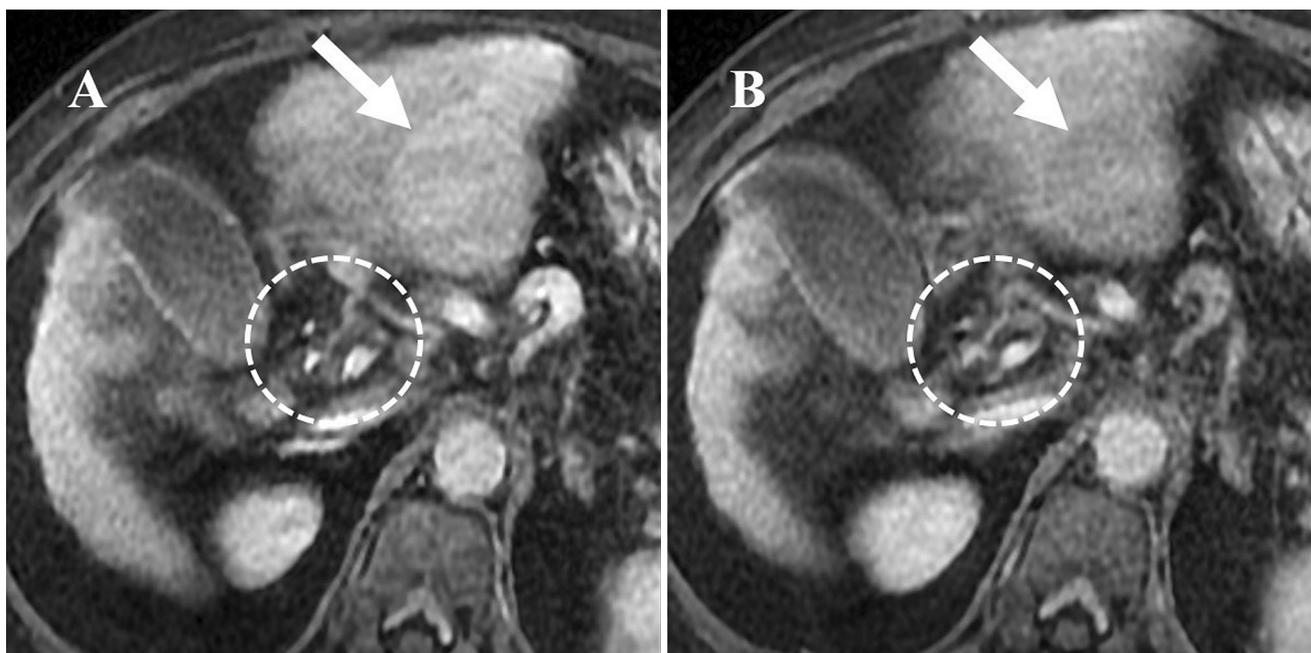
demonstrated diffuse positive stain for CK19 (**c**) which is typically seen in cholangiocarcinoma, and focal positive tumor cells for arginase (**d**), highly specific for HCC. The lesion was classified as a combined hepatocellular-cholangiocarcinoma.

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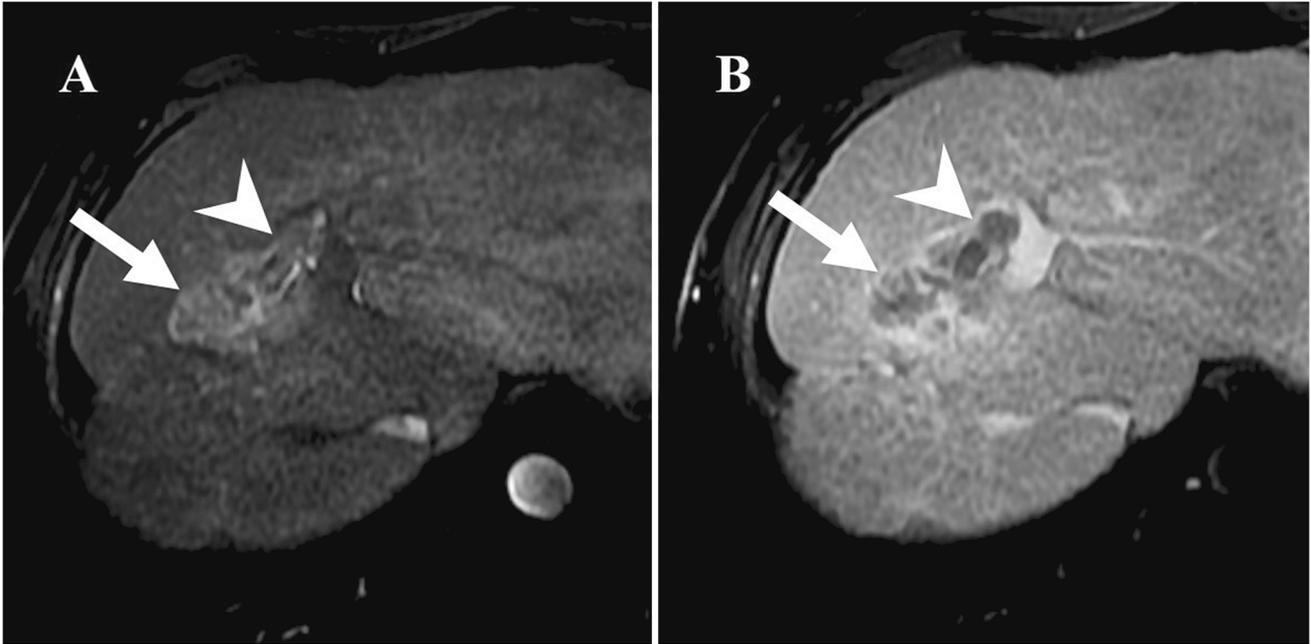
**Fig. 10.** 70-year-old male with HBV cirrhosis. Gadoxetate-MRI demonstrates a 3.8 cm heterogeneous rim-APHE observation on HAP (**a**) and persistent peripheral enhancement on PVP (**b**), thus classified as LR-M. Gross

specimen after resection (**c**) revealed a well-circumscribed firm lesion. Histological examination (not shown) confirmed a metastasis of colorectal origin.



**Fig. 11.** 75-year-old female with HCV cirrhosis. Gadoxetate-enhanced MRI demonstrates a 5.1 cm observation with non-rim APHE (arrow, **a**) and “washout” on PVP (arrow, **b**), compatible with a LR-5 observation. A sub-occlusive

thrombus in the extra-hepatic portal vein (circle on **a** and **b**) shows no enhancement on HAP and it is not in contiguity with the LR-5 observation. The thrombus was classified as “bland”.



**Fig. 12.** 50-year-old male with history of cirrhosis and HCC. Gadoxetate-enhanced MRI on HAP (a) shows a 3.2 cm APHE observation (arrow) with “washout” on PVP (b), compatible with a LR-5 observation. A thrombus in the right portal vein

(arrowhead, b) expands the vessel, it is in continuity with the LR-5 observation and shows arterial enhancement (arrowhead, a), compatible with tumor in vein (LR-TIV).



**Fig. 13.** 71-year-old male with recent diagnosis of a liver mass. Axial (a) and coronal (b) CT images obtained during the PVP demonstrate a 9.2 cm rim-enhancing observation with adjacent tumor in vein (white arrows) involving the right portal vein. In this case the tumor in vein is contiguous with a

targetoid mass with imaging favoring a non-HCC malignancy. Image of gross specimen after right lobectomy (c) shows an intra-hepatic cholangiocarcinoma extending into the lumen of the right portal vein (black arrow).

**Summary**

We have reported common pitfalls noted when applying the LI-RADS system in clinical practice. Awareness of these pitfalls is important to maintain a

high diagnostic accuracy and to direct the patient to the optimal management. These pitfalls also indicate concepts that require further education and potentially additional clarification in future versions of LI-RADS.

**Compliance with ethical standards**

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**Conflict of interest** The authors declare that they have no conflict of interests.

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**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** Statement of informed consent was not applicable since the manuscript does not contain any patient data.

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