Supplementary Online Content

Kim SY, An J, Lim Y, Han S, Lee J, et al. MRI with liver-specific contrast for surveillance of patients with cirrhosis at high risk of hepatocellular carcinoma [published online September 22, 2016]. *JAMA Oncology*. doi:10.1001/jamaoncol.2016.3147

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Magnetic resonance imaging categories and scoring criteria for hepatocellular carcinoma.

Diagnostic Categories	Scoring Criteria
Highly suggestive (Category 5)	One of the followings
	Size ≥ 1cm AND arterial enhancement AND low SI on portal or delay phase
	Definite tumor thrombus
Suspicious (Category 4)	One of the followings
	Size ≥ 1cm AND one or more of the followings
	Arterial enhancement AND low SI on HB phase
	Arterial enhancement AND T2 moderate high SI
	T2 moderate high SI AND low SI on portal, delayed, or HB phase
	low SI on portal AND low SI on HB phase
	Size < 1cm AND arterial enhancement AND low SI on portal, delayed, or HB phase
	Equivocal tumor thrombus
	Increase in size ≥ 1cm on F/U imaging in the lesion previously classified as Category 3
Equivocal (Category 3)	One of the followings
	Size ≥ 1cm AND only one of the followings
	T2 moderate high SI
	Low SI on portal phase
	Low SI on delayed phase
	Low SI on HB phase,
	Containing fat
	Capsular enhancement on Portal or Delayed phase
Probably benign (Category 2)	Imaging features suggestive of a benign entity*
Definitely benign (Category 1)	Imaging features diagnostic of a benign entity†

The likelihood of hepatocellular carcinoma (HCC) was based the Liver Imaging Reporting and Data System, version 1.0 (http://www.acr.org/Quality-Safety/Resources/LIRADS/Archive) after modifications.
F/U, follow-up; HB, hepatobiliary; MRI, magnetic resonance imaging; SI, signal intensity.
*Atypical cyst (or probable cyst), atypical hemangioma (or probable hemangioma), atypical focal fat deposition (or probable focal fat), atypical focal fat sparing (or probable focal fat sparing), hypertrophic pseudomass interpreted as probably benign, rounded perfusional alterations (nodular arterial phase hyperenhancement, NAPH), patchy (changed from "florid") perfusional alterations, atypical confluent fibrosis (probable confluent fibrosis), atypical focal scars (probable focal scars), some arterial-phase non-hyperenhancing atypical nodules progressively enhancing observations which do not meet the criteria in Category 3.
†Cyst, hemangioma, focal fat deposition, focal fat sparing, hypertrophic pseudomass interpreted as definitely benign, wedge-shaped perfusional alterations, confluent fibrosis, focal scars, homogeneous siderotic nodules.

eTable 2. Ultrasonography categories and scoring criteria for hepatocellular carcinoma.

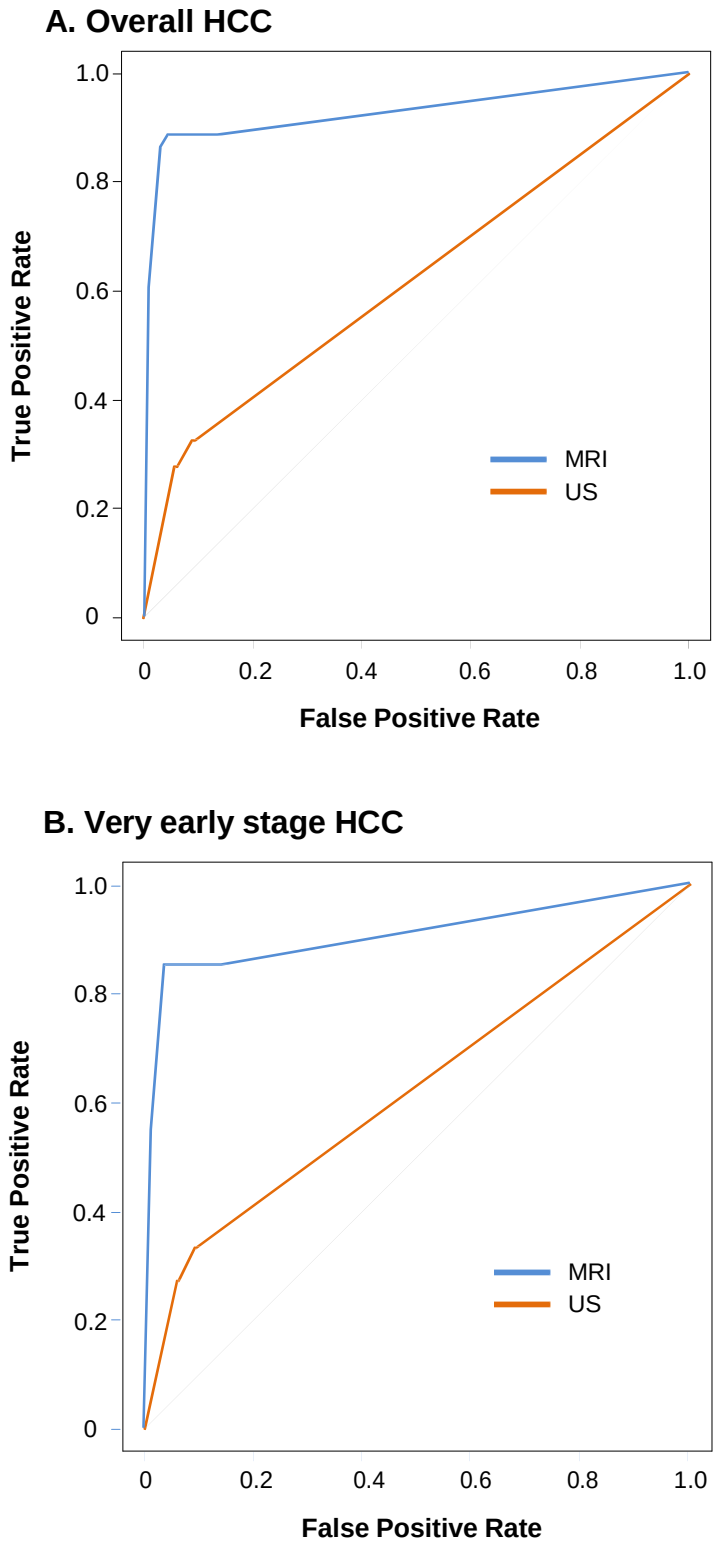
Diagnostic Categories	Scoring Criteria
Suspicious (Category 4)	One of the followings
	Size ≥ 1cm AND one or more of the followings
	Discrete focal mass distinguishable from the adjacent parenchyma
	Peripheral low echoic halo
	Mosaic pattern
	Definite tumor thrombus
Equivocal (Category 3)	Size < 1cm AND one or more of the followings
	Peripheral halo
	Mosaic pattern
	Thrombus (equivocal for benign or malignant)
Probably benign (Category 2)	Imaging features suggestive of a benign entity including cyst, hemangioma, focal fat deposition, focal fat sparing, or hypertrophic pseudomass
Definitely benign (Category 1)	Imaging features diagnostic of a benign entity including cyst, hemangioma, focal fat deposition, focal fat sparing, or hypertrophic pseudomass

The likelihood of hepatocellular carcinoma (HCC) was based on previous work[1-3] after modifications.

References)

1. Tanaka S, Kitamura T, Ohshima A, Umeda K, Okuda S, Ohtani T, Tatsuta M, Yamamoto K. Diagnostic accuracy of ultrasonography for hepatocellular carcinoma. Cancer. 1986 Jul 15;58(2):344-7.
2. Teefey SA, Hildeboldt CC, Dehdashti F, Siegel BA, Peters MG, Heiken JP, Brown JJ, McFarland EG, Middleton WD, Balfe DM, Ritter JH. Detection of primary hepatic malignancy in liver transplant candidates: prospective comparison of CT, MR imaging, US, and PET. Radiology. 2003 Feb;226(2):533-42.
3. Yu SC, Yeung DT, So NM. Imaging features of hepatocellular carcinoma. Clin Radiol. 2004 Feb;59(2):145-56.

eFigure 1. Receiver operating characteristic curves for US and MRI in the detection of overall and very early stage HCC



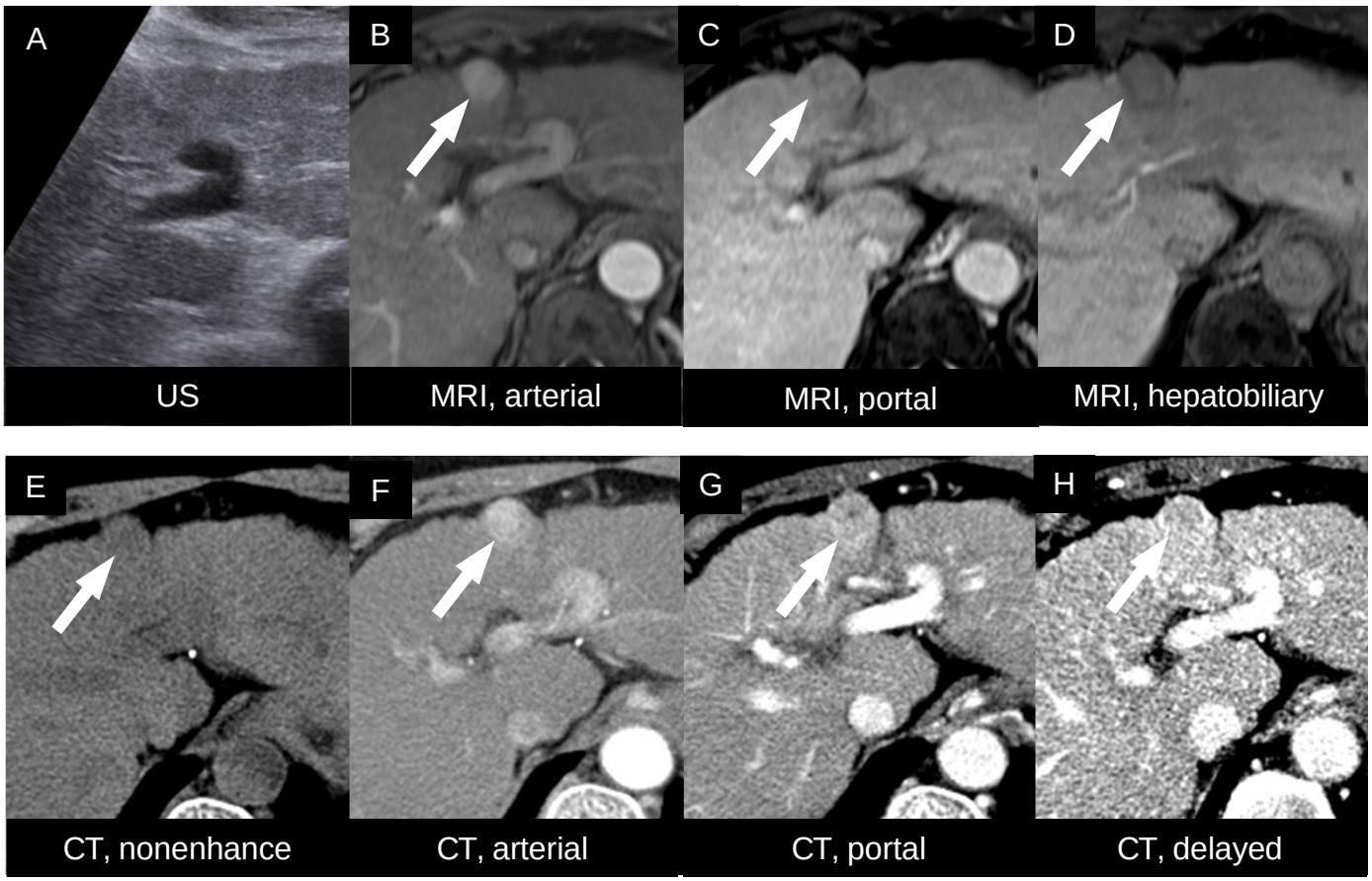
The difference between the area under the curves was significant between MRI and US in the detection of overall HCC (0.93 [95% CI, 0.87–0.98] vs. 0.62 [95% CI, 0.55–0.69]; *P*<.001) and very early stage HCC (0.90 [95% CI, 0.83–0.97] vs. 0.62 [95% CI, 0.54–0.71]; *P*<.001).

eTable 3. Factors associated with the false-negative findings of US to detect HCC nodules.

Characteristics	Visible nodules on US (n = 12)	Invisible nodules on US (n = 31)	*P*
No. of patients	12	31	
Age at diagnosis, years	62.8 ± 6.8	58.7 ± 6.9	.09
Male	9 (75.0%)	20 (64.5%)	.72
Body mass index	25.6± 3.5	24.1 ± 2.7	.15
Child-Pugh class A	8 (66.7%)	22 (71.0%)	>.99
Liver stiffness (kPa)	17.6 ± 6.1	16.8 ± 7.7	.77
Image factors			
Satisfactory US image quality	9 (75.0%)	23 (74.2%)	>.99
Satisfactory MRI image quality	12 (100%)	31 (100%)	NA
Tumor size* (cm)	1.7 ± 0.7	1.6 ± 0.7	.70
Hepatic dome location	2 (16.7%)	13 (45.2%)	.16
Subcapsular location	2 (16.7%)	18 (58.1%)	.02

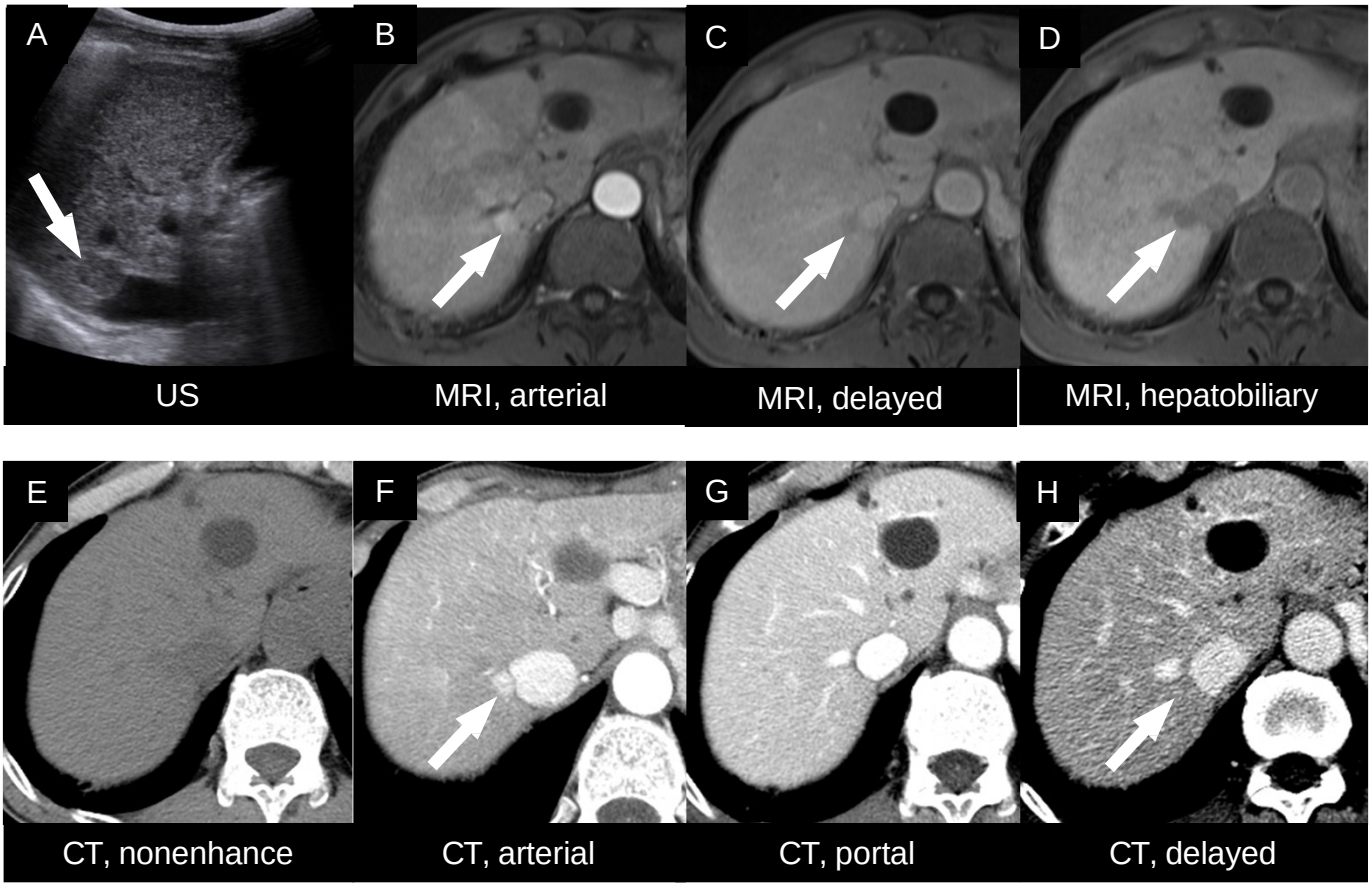
Data are n, n (%), or Mean ± standard deviation, unless otherwise specified.
HCC, hepatocellular carcinoma: MRI, magnetic resonance imaging: NA, not applicable: US, ultrasonography
* Maximum tumor diameter

eFigure 2. A representative patient with a HCC detected only by gadoxetic acid-enhanced MRI



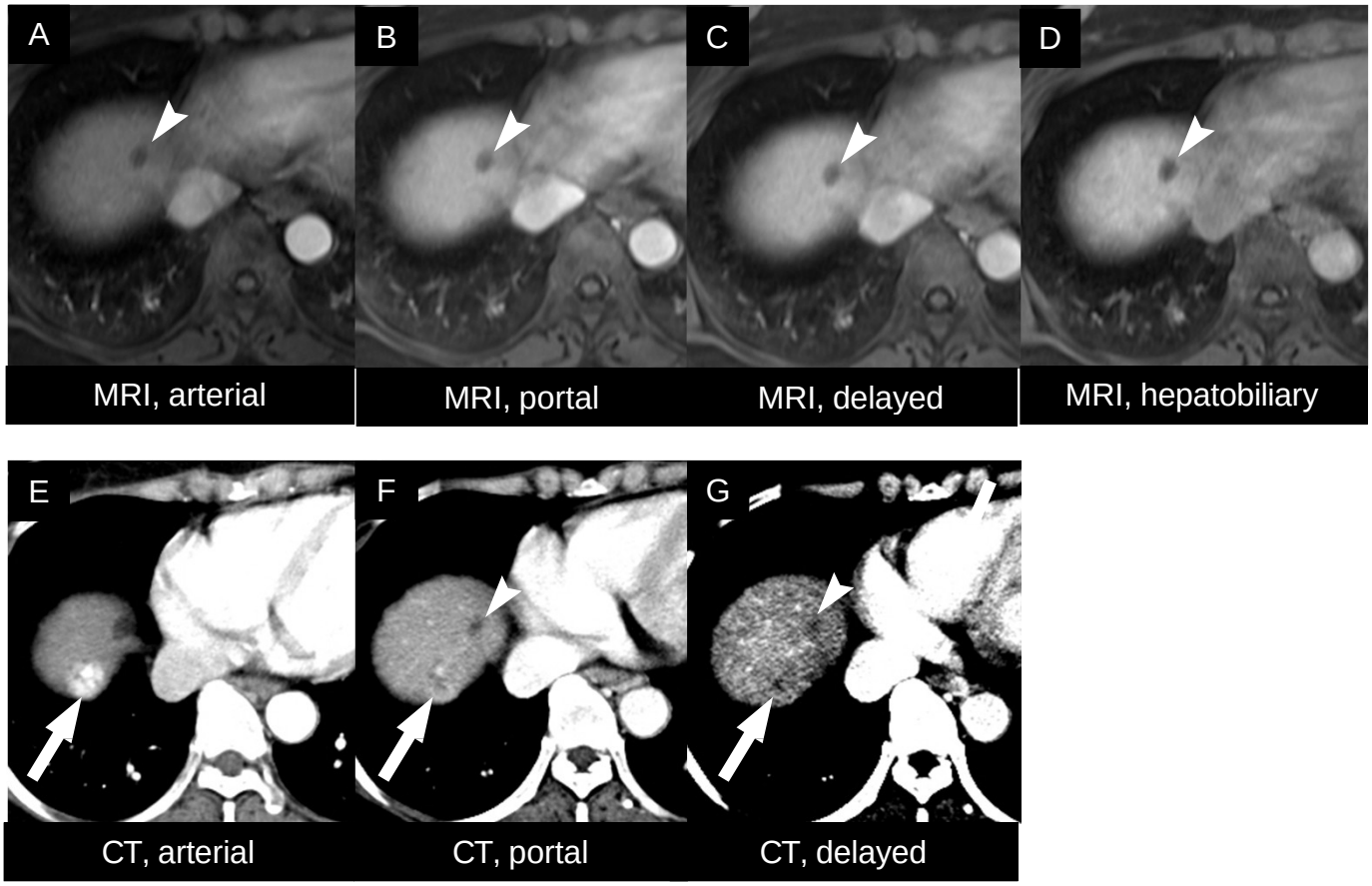
In this 72-year-old woman with hepatitis B-associated cirrhosis, US at Round 2 did not detect any lesions (A). However, gadoxetic acid-enhanced MRI at Round 2 identified a 1.6 cm-sized nodule in the subcapsular area of the left lobe of the liver with features highly suggestive HCC (category 5; B-D, indicated by arrows). A dynamic CT scan as a recall process demonstrated arterial hypervascularity and subtle delayed wash-out and capsular enhancement, and thus, categorized the lesion as HCC (E-H, indicated by arrows). The lesion was confirmed as HCC by surgical pathology.

eFigure 3. The patient with a HCC detected only by US



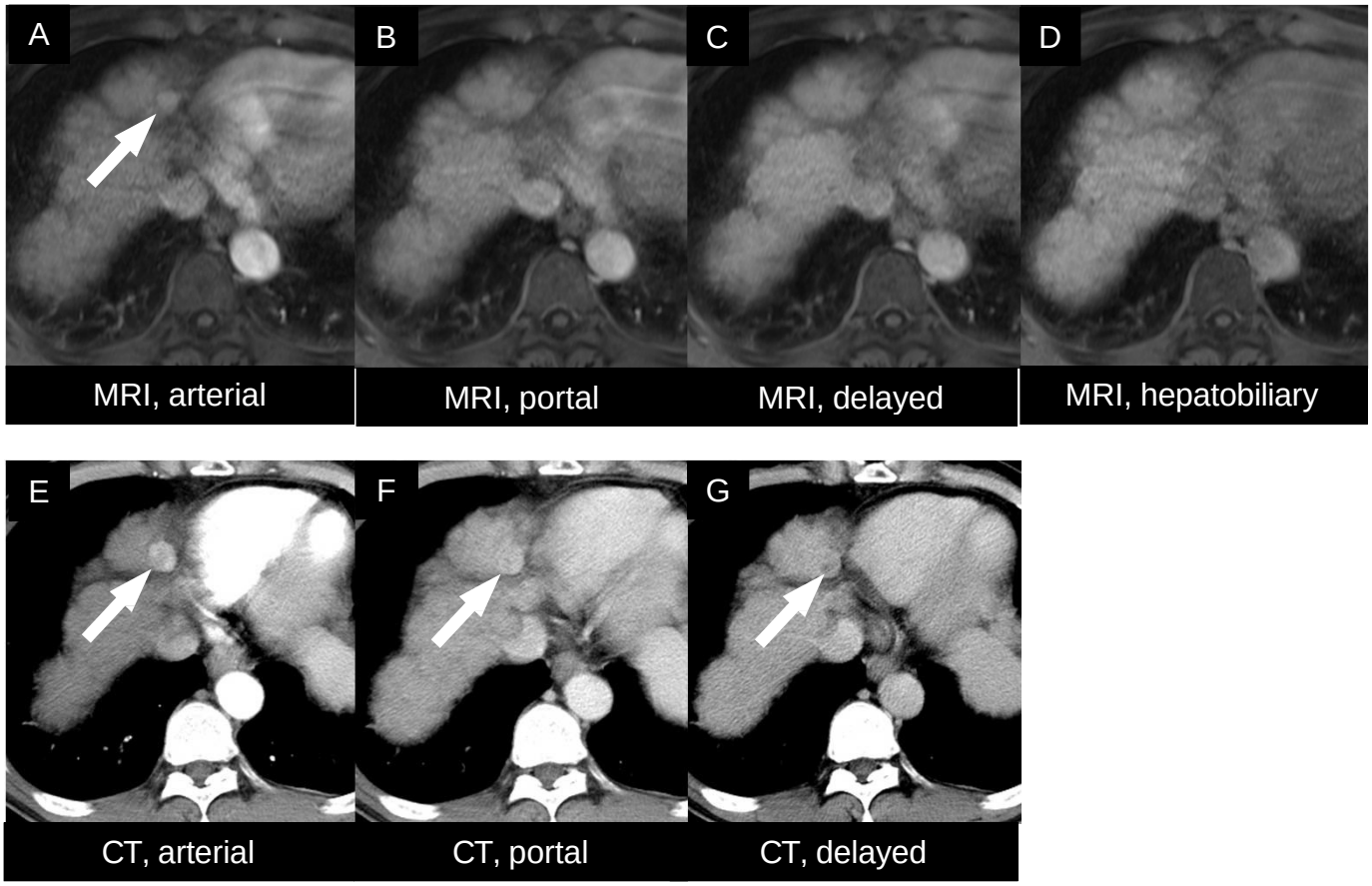
In this 63-year-old man with hepatitis C-associated cirrhosis, US at Round 1 found a 1.5 cm-sized hypoechoic lesion (indicated with arrow) (A). However, initial interpretation of Round 1 gadoxetic acid-enhanced MRI missed the lesion, as the lesion was located close to the inferior vena cava and right hepatic vein (B-D). The lesion could be identified on a retrospective review (B-D, indicated by arrows). A dynamic CT scan as a recall process demonstrated arterial hypervascularity and subtle wash-out on the delayed phase, and thus, the lesion was categorized as HCC (E-H, indicated by arrows).

eFigure 4. A representative patient with a HCC false negative both on US and MRI



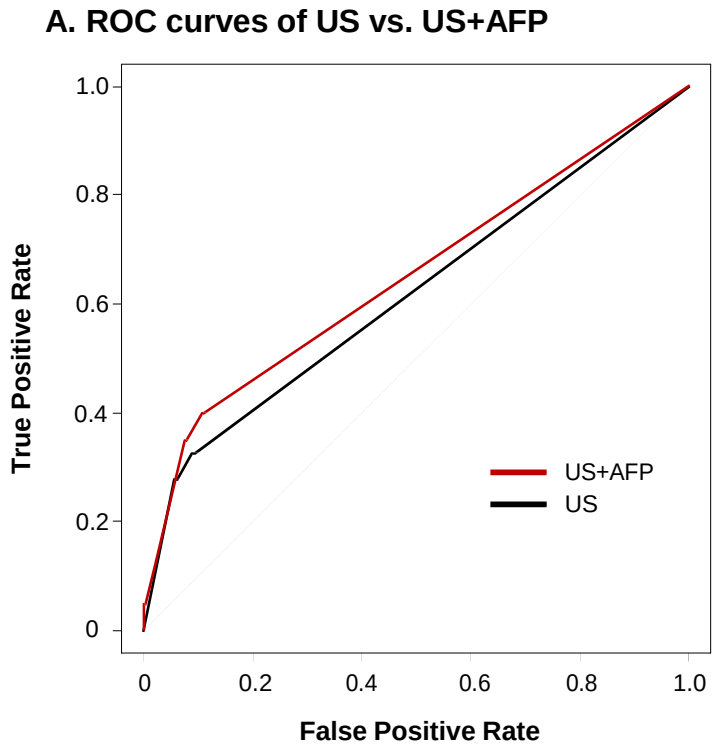
In this 56-year-old woman with hepatitis B-associated cirrhosis, Round 3 gadoxetic acid-enhanced MRI did not find any lesion suggestive of HCC (A-D). Another hypointense lesion in right lobe (A-D, indicated with arrowheads) was a hepatic cyst. However, the follow-up CT obtained 6 months after Round 3 MRI identified that a newly-developed 1.8 cm-sized lesion with arterial hypervascularity and wash-out on portal and delayed phase images (E-G, indicated with arrows). Therefore, the lesion was deemed to be incident HCC, which was confirmed later by surgical pathology. The hepatic cyst is also noted (E-G, indicated with arrowheads).

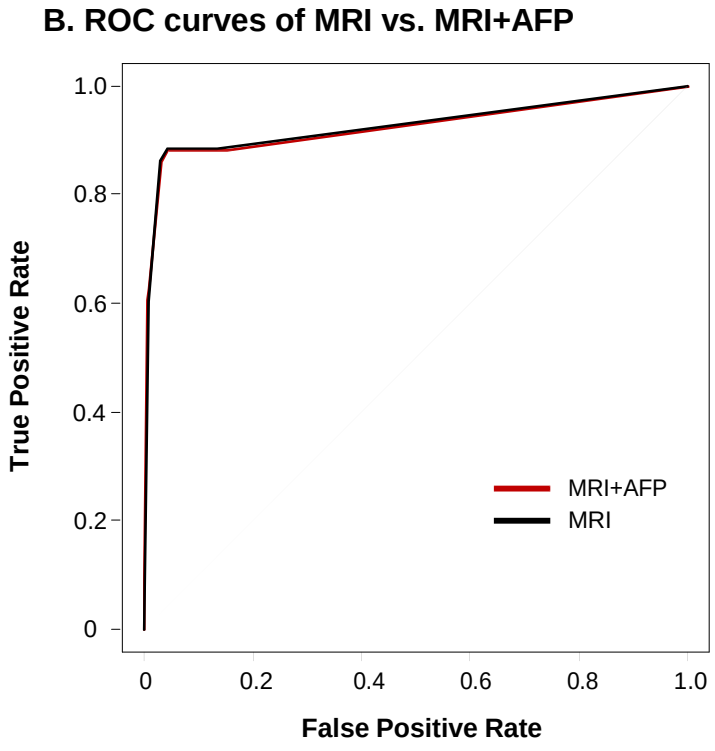
eFigure 5. A representative patient with a HCC false negative both on US and MRI



In this 61-year-old man with hepatitis B-associated cirrhosis, Round 3 gadoxetic acid-enhanced MRI detected a 1.2 cm-sized arterial hypervascular nodule (A, indicated with arrow) in right hepatic dome which showed isointensity on portal, delayed, and hepatobiliary phase images (B-D). Thus, the lesion was not regarded as HCC. However, the follow-up CT obtained 6 months after Round 3 MRI found that the lesion showed interval growth up to 1.6 cm in diameter, arterial hypervascularity and wash-out on delayed phase images (E-F, indicated with arrows). The lesion was diagnosed as HCC.

eFigure 6. Receiver operating characteristic curves for US and MRI with or without AFP in the detection of HCC





The difference in the area under the curves was significant between US+AFP and US alone (0.65 [95% CI, 0.57–0.73] vs. 0.62 [95% CI, 0.55–0.69]; *P*=.049), while it was not significant between MRI+AFP and MRI alone (0.93 [95% CI, 0.87–0.98] vs. 0.93 [95% CI, 0.87–0.98]; *P*=.99). The positive screening value of AFP was defined as >20 ng/mL.