

American College of Radiology
ACR Appropriateness Criteria®
Staging and Follow-up of Primary Liver Cancer

Variant: 1 Adult. Primary liver cancer. Screening.

Procedure	Appropriateness Category	Relative Radiation Level
US abdomen	Usually Appropriate	O
MRI abdomen without and with IV contrast	May Be Appropriate	O
MRI abdomen without IV contrast	May Be Appropriate	O
CT abdomen with IV contrast multiphase	May Be Appropriate	⊕⊕⊕⊕
US abdomen with IV contrast	Usually Not Appropriate	O
MRI abdomen without and with IV contrast with MRCP	Usually Not Appropriate	O
MRI abdomen without IV contrast with MRCP	Usually Not Appropriate	O
CT abdomen with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT abdomen without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT abdomen without and with IV contrast	Usually Not Appropriate	⊕⊕⊕⊕
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	⊕⊕⊕⊕

Variant: 2 Adult. Primary liver cancer. Staging.

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with IV contrast	Usually Appropriate	O
CT abdomen with IV contrast multiphase	Usually Appropriate	⊕⊕⊕⊕
MRI abdomen without and with IV contrast with MRCP	May Be Appropriate	O
Bone scan whole body	May Be Appropriate	⊕⊕⊕
CT abdomen and pelvis with IV contrast	May Be Appropriate (Disagreement)	⊕⊕⊕
CT chest with IV contrast	May Be Appropriate (Disagreement)	⊕⊕⊕
CT chest without IV contrast	May Be Appropriate (Disagreement)	⊕⊕⊕
CT pelvis with IV contrast	May Be Appropriate	⊕⊕⊕
US abdomen transabdominal	Usually Not Appropriate	O
US abdomen with IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast with MRCP	Usually Not Appropriate	O
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	⊕⊕⊕
CT chest without and with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT pelvis without IV contrast	Usually Not Appropriate	⊕⊕⊕
FDG-PET/MRI skull base to mid-thigh	Usually Not Appropriate	⊕⊕⊕
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	⊕⊕⊕⊕
CT pelvis without and with IV contrast	Usually Not Appropriate	⊕⊕⊕⊕

Variant: 3 Adult. Primary liver cancer. Liver observations under active surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with IV contrast	Usually Appropriate	O
CT abdomen with IV contrast multiphase	Usually Appropriate	⊕⊕⊕⊕

MRI abdomen without and with IV contrast with MRCP	May Be Appropriate	O
CT abdomen without and with IV contrast	May Be Appropriate	⊕⊕⊕⊕
US abdomen transabdominal	Usually Not Appropriate	O
US abdomen with IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast with MRCP	Usually Not Appropriate	O
CT abdomen with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT abdomen without IV contrast	Usually Not Appropriate	⊕⊕⊕
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	⊕⊕⊕⊕

Variant: 4 Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with IV contrast	Usually Appropriate	O
CT abdomen with IV contrast multiphase	Usually Appropriate	⊕⊕⊕⊕
CT abdomen without and with IV contrast	Usually Appropriate	⊕⊕⊕⊕
MRI abdomen without and with IV contrast with MRCP	May Be Appropriate	O
US abdomen transabdominal	Usually Not Appropriate	O
US abdomen with IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast with MRCP	Usually Not Appropriate	O
CT abdomen with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT abdomen without IV contrast	Usually Not Appropriate	⊕⊕⊕
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	⊕⊕⊕⊕

Variant: 5 Adult. Primary liver cancer. Treated. Routine surveillance.

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with IV contrast	Usually Appropriate	O
CT abdomen with IV contrast multiphase	Usually Appropriate	⊕⊕⊕⊕
MRI abdomen without and with IV contrast with MRCP	May Be Appropriate	O
CT abdomen without and with IV contrast	May Be Appropriate	⊕⊕⊕⊕
US abdomen transabdominal	Usually Not Appropriate	O
US abdomen with IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast	Usually Not Appropriate	O
MRI abdomen without IV contrast with MRCP	Usually Not Appropriate	O
CT abdomen with IV contrast	Usually Not Appropriate	⊕⊕⊕
CT abdomen without IV contrast	Usually Not Appropriate	⊕⊕⊕
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	⊕⊕⊕⊕

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Summary of Literature Review

Introduction/Background

Liver cancer is an increasing challenge to global health with continually increasing incidence despite recent advancements. Liver cancer is the sixth most common cancer worldwide, with 905,677 new cases in 2020, and is the third leading cause of cancer-related deaths globally [1]. Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer and accounts for approximately 75% to 85% of cases [1]. Of these cases, 90% occur in the setting of chronic liver disease. Infection with hepatitis B virus is the leading risk factor for HCC development worldwide and is estimated to be responsible for approximately 56% of cases [1]. In the United States, the most common risk factor is infection with hepatitis C. Despite advancements in oral therapies for the treatment of hepatitis C, patients with cirrhosis are at a persistent high risk after achieving sustained virologic response and clearance of the virus [2]. Metabolic dysfunction-associated steatohepatitis, previously nonalcoholic steatohepatitis (NASH), is now the fastest growing etiology of HCC due to its increased prevalence. Chronic alcohol consumption is another leading risk factor. Less prevalent risk factors include primary biliary cholangitis, hemochromatosis, and α 1-antitrypsin deficiency. Surveillance Epidemiology End Results reported HCC as the fastest increasing cause of cancer-related death in the United States since 2000, and HCC is projected to become the third leading cause of cancer-related death if trends continue [2]. Prognosis varies widely, with a 5-year survival exceeding 70% in patients who are diagnosed with early-stage HCC, compared with a median survival of 1 to 2 years in those diagnosed at more advanced stages [3].

Several alternative HCC staging systems have been previously proposed. These include the Barcelona Clinic Liver Cancer (BCLC) criteria, Cancer of the Liver Italian Program, Japan Integrated Staging, and Chinese University Prognostic Index, among others. According to the 2018 Practice Guidance by the American Association for the Study of Liver Diseases (AASLD), the BCLC staging system should be used [4]. This system uses the patient's Child-Pugh score, number and size of nodules, Eastern Cooperative Oncology Group score, portal vein invasion, nodal status, and extrahepatic metastatic disease to stratify patients into stages. In 2008, the first Liver Imaging-Reporting and Data System (LI-RADS) committee convened, with support from the ACR. This committee formed to standardize the lexicon, imaging interpretation, and the reporting of findings to improve communication and diagnosis of HCC in high-risk patients [5]. Since 2008, there have been several major updates to LI-RADS, most recently in 2018. The LI-RADS assigns a diagnostic category to each liver observation, which reflects the level of suspicion for HCC. The only blood-based biomarker currently validated for HCC surveillance is α -fetoprotein (AFP). Of note, AFP can at times be nonspecific, with elevation also seen in acute hepatitis, cholangiocarcinoma, and extrahepatic pathologies, as well [6]. Ultimately, the management of HCC encompasses multiple disciplines including hepatologists, diagnostic radiologists, pathologists, transplant surgeons, surgical oncologists, radiation oncologists, and more. The development of a multidisciplinary clinic with dedicated tumor board review has been shown to increase survival in these patients with HCC [4].

Special Imaging Considerations

Since 2011, LI-RADS has published technical guidelines for the performance and interpretation of

multiphase CT, MRI, ultrasound (US), and contrast-enhanced US (CEUS) examinations. Please consult these technical guidelines for specific imaging considerations [7].

Discussion of Procedures by Variant

Variant 1: Adult. Primary liver cancer. Screening.

Pre-existing cirrhosis is found in >80% of patients diagnosed with HCC. Therefore, any etiology that can lead to chronic liver injury and eventually cirrhosis should be considered a risk factor for HCC. The decision to enter a patient into screening is determined by the level of risk for HCC, as well as the patient's age, overall health, functional status, and willingness to comply with surveillance requirements. Because the goal of imaging screening is to increase survival through early HCC diagnosis, screening should only be performed on patients who are eligible for HCC-related treatments. Guidelines across scientific societies agree that screening should be performed semiannually, as imaging at 6-month intervals yields improved survival [6].

Variant 1: Adult. Primary liver cancer. Screening.

A. CT abdomen with IV contrast

Despite high diagnostic performance, there is a lack of evidence on the use of contrast-enhanced CT for the screening of patients at risk for development of HCC. However, in select patients with inadequate US examinations, CT may be used [4]. The phenomenon of arterial hyperenhancement and delayed washout has a sensitivity of 89% and specificity of 96% for the diagnosis of HCC and is therefore considered the radiographic hallmark [5]. Because of these imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal, whereas single-phase CT does not allow for adequate lesion characterization.

Variant 1: Adult. Primary liver cancer. Screening.

B. CT abdomen with IV contrast multiphase

Despite high diagnostic performance, there is a lack of evidence on the use of contrast-enhanced CT for the screening of patients at risk for development of HCC. However, in select patients with inadequate US examinations, CT may be used [4].

The phenomenon of arterial hyperenhancement and delayed washout has a sensitivity of 89% and specificity of 96% for the diagnosis of HCC and is therefore considered the radiographic hallmark [5]. Because of these imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal.

Variant 1: Adult. Primary liver cancer. Screening.

C. CT abdomen without and with IV contrast

Despite high diagnostic performance, there is a lack of evidence on the use of contrast-enhanced CT for the screening of patients at risk for development of HCC [4]. There is a lack of evidence to support the addition of noncontrast phase in this setting.

Variant 1: Adult. Primary liver cancer. Screening.

D. CT abdomen without IV contrast

Difficulties evaluating for potential underlying masses without the use of intravenous (IV) contrast limit the usefulness of noncontrast CT in screening for HCC.

Variant 1: Adult. Primary liver cancer. Screening.

E. FDG-PET/CT skull base to mid-thigh

There is limited literature supporting the use of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT in screening patients for primary liver cancer.

Variant 1: Adult. Primary liver cancer. Screening.

F. MRI abdomen without and with IV contrast

Kim et al [8] published a cohort study of 407 patients with cirrhosis and compared US with MRI with liver-specific contrast for the surveillance of HCC. A total of 43 patients developed HCC, with 1 detected by US only, 26 by MRI alone, 11 by both, and 5 missed by both modalities. MRI had a lower false-positive rate than US (3% versus 5.6%).

To maximize value, abbreviated MRI examination protocols have been developed and are being tested. One potential abbreviated protocol, which has been proposed and studied, includes obtaining only T1-weighted hepatobiliary phase axial images in addition to T2-weighted single-shot fast spin-echo axial images. These protocols can achieve sensitivities of 80% to 90% and specificities of 91% to 98% in small cohort studies [9,10].

Demirtas et al [11] evaluated the effectiveness of annual contrast-enhanced MRI in screening at-risk patients when compared with US. Using the evidence of 294 patients with consistent annual contrast-enhanced MRI and biannual AFP surveillance between 2008 and 2017. Thirty-five (11.9%) HCCs were detected with annual surveillance MRI. Of these, 30 (85.8%) were early-stage and 15 (42.9%) were very early-stage. MRI had a sensitivity of 83.3% and 80%, with a specificity of 95.4% and 91.4% for detecting early and very early-stage HCCs, respectively.

Kim et al [9] also evaluated screening using MRI with liver-specific contrast agents. A total of 407 eligible patients received 1,100 screenings with paired US and MRI. HCCs were diagnosed in 43 patients: 1 detected by US only, 26 by MRI only, 11 by both, and 5 were missed by both. The HCC detection rate of MRI was 86.0% (37/43), significantly higher than the 27.9% (12/43) of US ($P < .001$). MRI showed a significantly lower rate of false-positive findings than US (3.0% versus 5.6%; $P = .004$). Of the 43 patients with HCC, 32 (74.4%) had very early-stage HCC (a single nodule < 2 cm), and 29 (67.4%) received curative treatments.

As these studies demonstrate, MRI may be a screening option for patients with poor visualization on US screening examinations.

Variant 1: Adult. Primary liver cancer. Screening.

G. MRI abdomen without and with IV contrast with MRCP

There is no evidence for the addition of MR cholangiopancreatography (MRCP) sequences to an MR abdomen without and with IV contrast for the purpose of screening for HCC.

Variant 1: Adult. Primary liver cancer. Screening.

H. MRI abdomen without IV contrast

Sutherland et al [12] evaluated an abbreviated noncontrast MRI protocol compared with screening US. Patients with chronic liver disease referred for US screening underwent a liver US and a liver MRI comprising free breathing diffusion-weighted imaging. One hundred and ninety-two patients were recruited, and HCC was diagnosed in 6 patients (3%), all of whom were detected at US screening, and 5 detected at MRI screening. US had false-positive studies 20 times (10%), whereas diffusion-weighted MRI had 3 false-positive examinations (2%, $P \geq .05$). The sensitivity, specificity, positive predictive value, and negative predictive values for US are 100%, 90%, 23%, and 100%, respectively, although for MRI they were 83%, 98%, 63%, and 99%, respectively.

Kim et al [8] are currently conducting the magnetic resonance imaging as surveillance tools for hepatocellular carcinoma (MAGNUS-HCC) trial, which is the comparison of biannual US and annual noncontrast MRI as surveillance tools. The date of trial registration was September 15, 2015, and evidence collection is still ongoing.

Variant 1: Adult. Primary liver cancer. Screening.

I. MRI abdomen without IV contrast with MRCP

There is no evidence for the addition of MRCP sequences to an MR abdomen without IV contrast for the purpose of screening for HCC.

Variant 1: Adult. Primary liver cancer. Screening.

J. US abdomen

The AASLD currently recommends surveillance using US, with serum AFP, every 6 months [4]. The European Association for the Study of the Liver guidelines also recommend surveillance with US every 6 months [13].

Zhang et al [14] conducted a large randomized controlled trial of 18,000+ patients with hepatitis B. The screened group completed 58.2% of the screening offered. When the screening group was compared with the control group, the number of HCC was 86 versus 67; subclinical HCC being 52 (60.5%) versus 0; small HCC 39 (45.3%) versus 0; resection achieved 40 (46.5%) versus 5 (7.5%); 1-, 3-, and 5-year survival rate 65.9%, 52.6%, 46.4% versus 31.2%, 7.2%, 0%, respectively. Thirty-two people died from HCC in the screened group versus 54 in the control group, and the HCC mortality rate was significantly lower in the screened group than in controls, being 83.2/100,000 and 131.5/100,000, respectively, with a mortality rate ratio of 0.63 (95% confidence interval, 0.41-0.98). Overall findings indicated that biannual screening reduced HCC mortality by 37%.

Moon et al [15] found in a matched case-control study of the Veterans Affairs health care system that screening patients with cirrhosis using US, a measurement of serum AFP, either test, or both tests was not associated with decreased HCC-related mortality.

Recent evidence has suggested that US is operator-dependent and has poor performance in patient subgroups such as those with obesity and NASH [16]. In these patients with poor visualization, CT or MRI can be considered.

US LI-RADS provides a unified lexicon, precise interpretive criteria, standardized reporting, and follow-up recommendations for US surveillance in patients at-risk for HCC [17].

Variant 1: Adult. Primary liver cancer. Screening.

K. US abdomen with IV contrast

CEUS is not useful as a sole means of screening for HCC but may be a valuable screening modality in the future. Notably, this modality could help reduce the number of return visits for a follow-up examination if an incidental liver lesion is detected on grayscale US, with potential immediate administration of US contrast for lesion characterization [18]. However, contrast-enhanced studies often have limitations in complete visualization of the liver; there is limited evidence to demonstrate the usefulness of CEUS as a main screening examination.

Variant 2: Adult. Primary liver cancer. Staging.

Because HCC occurs in an identifiable at-risk patient population, many patients are diagnosed with

a suspicious lesion during screening. However, due to under-implementation of screening, particularly in developing countries, up to 50% of cases are diagnosed incidentally, usually identified on cross-sectional imaging performed for other reasons [6]. Once a suspicious lesion is identified, patients often undergo further testing to establish a diagnosis. With multiphase CT and MRI, observations are assigned LI-RADS categories reflecting their relative probability of being benign, HCC, or other hepatic neoplasms. LI-RADS 5 lesions are definite HCC—and these imaging criteria are consistent with the Organ Procurement and Transplantation Network (OPTN) Class 5 criteria and the 2011 AASLD criteria [4]. After imaging or pathological diagnosis of HCC has been established, for complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19].

Variant 2: Adult. Primary liver cancer. Staging.

A. Bone scan whole body

If there is a suspicious osseous lesion on cross-sectional imaging, a bone scan may be of benefit to confirm osseous metastatic disease. There is no literature to support the routine usage of bone scans for the staging of every patient with primary liver cancer. Bone is the third most common site of metastasis, following the lung and abdominal lymph nodes [19].

Variant 2: Adult. Primary liver cancer. Staging.

B. CT abdomen and pelvis with IV contrast

The phenomenon of arterial hyperenhancement and delayed washout has a sensitivity of 89% and specificity of 96% for the diagnosis of HCC and is therefore considered the radiographic hallmark [5]. Because of these imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal. The AASLD recommends multiphase CT or multiphase MRI with extracellular or hepatobiliary agents for diagnostic evaluation because of similar performance characteristics [4].

If a CT abdomen with IV contrast multiphase or an MRI abdomen without and with IV contrast has been performed to diagnose HCC, a repeat of these examinations is unnecessary for staging purposes. However, if the diagnosis of HCC was made by CEUS or current multiphase imaging of the entire liver has not been performed, then CT abdomen with IV contrast multiphase or an MRI abdomen without and with IV contrast may be appropriate.

Variant 2: Adult. Primary liver cancer. Staging.

C. CT abdomen and pelvis without and with IV contrast

During the initial characterization of a liver lesion, due to the diagnostic hallmarks of HCC, a single postcontrast phase would be of less benefit.

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19].

Variant 2: Adult. Primary liver cancer. Staging.

D. CT abdomen and pelvis without IV contrast

The addition of a noncontrast sequence is usually most beneficial in the setting of postliver-directed therapy, and there is limited evidence on its usefulness in pretreatment staging.

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19].

Variant 2: Adult. Primary liver cancer. Staging.

E. CT abdomen with IV contrast multiphase

Difficulties evaluating for potential underlying masses without the use of IV contrast limit the usefulness of noncontrast CT for HCC staging.

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19].

Variant 2: Adult. Primary liver cancer. Staging.

F. CT chest with IV contrast

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19]. There is insufficient evidence regarding the use of IV contrast in evaluating for thoracic metastases in the setting of HCC; however, the advantage of IV contrast when imaging the chest relates to the improved conspicuity of thoracic adenopathy.

Variant 2: Adult. Primary liver cancer. Staging.

G. CT chest without and with IV contrast

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19]. There is insufficient evidence in the literature on the usage of contrast to suggest a without phase would be beneficial in this staging.

Variant 2: Adult. Primary liver cancer. Staging.

H. CT chest without IV contrast

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19]. There is insufficient evidence regarding the use of IV contrast in evaluating for thoracic metastases in the setting of HCC; however, the advantage of IV contrast when imaging the chest relates to the improved conspicuity of thoracic adenopathy.

Variant 2: Adult. Primary liver cancer. Staging.

I. CT pelvis with IV contrast

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19]. In patients whose imaging has been limited to the abdomen, the addition of a pelvic CT may be indicated for complete staging purposes. IV contrast may be helpful to identify metastatic adenopathy and peritoneal implants.

Variant 2: Adult. Primary liver cancer. Staging.

J. CT pelvis without and with IV contrast

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19]. In patients whose imaging has been limited to the abdomen, the addition of a pelvic CT may be indicated for complete staging purposes. There is insufficient evidence in the literature on the usage of contrast to suggest a without phase would be beneficial in this staging.

Variant 2: Adult. Primary liver cancer. Staging.

K. CT pelvis without IV contrast

For complete staging and consideration for liver transplantation, OPTN requires a chest CT to rule out metastatic disease [19]. In patients whose imaging has been limited to the abdomen, the addition of a pelvic CT may be indicated for complete staging purposes. IV contrast may be helpful to identify metastatic adenopathy and peritoneal implants.

Variant 2: Adult. Primary liver cancer. Staging.

L. FDG-PET/MRI skull base to mid-thigh

Staging according to the BCLC classification is based on conventional imaging. FDG-PET has been proposed to play a role in the detection of poorly differentiated HCC; however, its use is limited by its inability to detect well-differentiated HCC. Therefore, it is not currently recommended for HCC staging [20,21].

Dual tracer PET/CT has been validated for pretransplant staging for HCC. C11-acetate is used, as it is sensitive for well-differentiated HCC, in conjunction with FDG [22].

Variant 2: Adult. Primary liver cancer. Staging.

M. MRI abdomen without and with IV contrast

The phenomenon of arterial hyperenhancement and delayed washout has a sensitivity of 89% and specificity of 96% for the diagnosis of HCC and is therefore considered the radiographic hallmark [5]. Because of these imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal. The AASLD recommends multiphase CT or multiphase MRI with extracellular or hepatobiliary agents for diagnostic evaluation because of similar performance characteristics [4].

A recent meta-analysis reported that the sensitivity of MRI with extracellular or hepatobiliary agents exceeded that of CT [23]. For all tumor sizes, the 19 comprehensive comparisons showed significantly higher sensitivity (82% versus 66%) and lower negative likelihood ratio (0.20 versus 0.37) for MRI over CT. However, this advantage was not sufficient to definitively recommend MRI due to low quality of reviewed evidence and many factors that go into modality selection for each patient [23].

There is currently insufficient evidence to recommend either extracellular contrast or hepatobiliary contrast over the other [4].

If a CT abdomen with IV contrast multiphase or an MRI abdomen without and with IV contrast has been performed to diagnose HCC, a repeat of these examinations is unnecessary for staging purposes. However, if the diagnosis of HCC was made by CEUS or current multiphase imaging of the entire liver has not been performed, then CT abdomen with IV contrast multiphase or an MRI abdomen without and with IV contrast may be appropriate.

Variant 2: Adult. Primary liver cancer. Staging.

N. MRI abdomen without and with IV contrast with MRCP

There is a lack of evidence for the addition of MRCP sequences to an MR abdomen without and with IV contrast for the purpose of staging HCC.

Variant 2: Adult. Primary liver cancer. Staging.

O. MRI abdomen without IV contrast

HCC staging requires the use of IV contrast.

Variant 2: Adult. Primary liver cancer. Staging.

P. MRI abdomen without IV contrast with MRCP

There is a lack of evidence for the addition of MRCP sequences to an MR abdomen without IV contrast for the purpose of staging HCC.

Variant 2: Adult. Primary liver cancer. Staging.

Q. US abdomen transabdominal

There is no evidence to support the use of transabdominal US in pretreatment staging of HCC.

Variant 2: Adult. Primary liver cancer. Staging.

R. US abdomen with IV contrast

CEUS does not provide a complete evaluation for nodal and distant metastatic disease and would not adequately stage a patient according to the BCLC criteria. It is also not suitable for staging the entire liver [17].

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

The designation of LI-RADS 3 for an observation, indicates a low probability of HCC. The differential diagnosis for these lesions includes benign and malignant entities, such as vascular pseudolesions and small HCCs. LI-RADS 4 lesions indicate probable HCC but do not meet all imaging criteria for definitive HCC diagnosis by imaging. The differential of these lesions includes dysplastic nodules, other benign entities, and rarely, non-HCC malignancies [4]. Because these lesions could represent small HCCs, but do not meet imaging criteria for definite HCC diagnosis and treatment, it is recommended that lesions >10 mm merit close cross-sectional imaging follow-up for a maximum of 18 months. The choice of observation with follow-up imaging versus treatment depends on several factors, including patient preference, anticipated follow-up time, rate of growth of the lesion, degree of liver decompensation, and AFP [4]. When active surveillance is elected, the goal of imaging is to identify any changes in a LI-RADS 3 lesion that would confirm HCC or to identify enlarging LI-RADS 4 lesions as early as possible.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

A. CT abdomen with IV contrast

The phenomenon of arterial hyperenhancement and delayed washout has a sensitivity of 89% and specificity of 96% for the diagnosis of HCC and is therefore considered the radiographic hallmark [5]. Because of these imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal, whereas single-phase CT does not allow for adequate lesion characterization.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

B. CT abdomen with IV contrast multiphase

The phenomenon of arterial hyperenhancement and delayed washout has a sensitivity of 89% and specificity of 96% for the diagnosis of HCC and is therefore considered the radiographic hallmark [5]. Because of these imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

C. CT abdomen without and with IV contrast

There is a lack of evidence supporting CT abdomen without and with IV contrast usefulness in the setting of active surveillance of the liver. However, in patients who have undergone prior liver-directed therapy, the addition of a noncontrast series may be appropriate.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

D. CT abdomen without IV contrast

Difficulties evaluating for potential underlying masses without the use of IV contrast limits the usefulness of noncontrast CT in the surveillance of LI-RADS 3 and 4 lesions.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

E. FDG-PET/CT skull base to mid-thigh

There is a lack of evidence supporting the use of FDG-PET in active surveillance for HCC.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

F. MRI abdomen without and with IV contrast

The phenomenon of arterial hyperenhancement and delayed washout has a sensitivity of 89% and specificity of 96% for the diagnosis of HCC and is therefore considered the radiographic hallmark [5]. Because of these imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

G. MRI abdomen without and with IV contrast with MRCP

There is no relevant literature to support the addition of MRCP sequences to an MRI abdomen without and with IV contrast in active surveillance for HCC. In patients with a history of biliary disease, an MRCP sequence may be appropriate to include.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

H. MRI abdomen without IV contrast

Difficulties evaluating for potential underlying masses without the use of IV contrast limit the usefulness of noncontrast MRI in the surveillance of LI-RADS 3 and 4 lesions.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

I. MRI abdomen without IV contrast with MRCP

There is no relevant literature to support the addition of MRCP sequences to an MRI abdomen without IV contrast in active surveillance for HCC.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

J. US abdomen transabdominal

In the setting of a mass lesion <1 cm in diameter detected on US screening, short-term follow-up with repeat US in 3 months is sufficient due to the small size, which makes characterization on cross-sectional imaging difficult [6]. However, for lesions ≥ 1 cm, there is insufficient evidence to support the use of US for active surveillance.

Variant 3: Adult. Primary liver cancer. Liver observations under active surveillance.

K. US abdomen with IV contrast

Surveillance with CEUS can be evaluated for changes in lesion microcirculation and can show evolving hepatocarcinogenesis. CEUS also has the added benefit of superior temporal resolution compared with that of CT and MRI. CEUS LI-RADS was developed to standardize imaging technique, interpretation, and reporting [17]. However, CEUS is limited for certain patients because only 1 or 2 lesions can be evaluated during the examination, and there may be incomplete visualization of the entire liver.

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

Patients with early-stage HCC as characterized by the BCLC staging system are preferred candidates for resection, transplantation, and local ablation. Ablation includes radiofrequency ablation, microwave ablation, and additional ablation techniques such as irreversible electroporation. Patients with intermediate stage are first candidates for transarterial chemoembolization (TACE) or transarterial radiotherapy. Those with advanced disease will receive systemic therapy [6]. Additionally, neoadjuvant therapies such as TACE or ablation are sometimes

used to prevent tumor progression as patients await transplantation ("bridging therapy"). External beam radiation therapy can also play a role in select patients, particularly in those with small tumors and who are not amenable to resection or transplantation [6].

In the setting of liver-directed or neoadjuvant systemic therapy, short-term immediate serial follow-up imaging is performed to evaluate treatment response and to determine whether patients may require retreatment. Response to postliver-directed therapy can be evaluated on imaging using the LI-RADS posttreatment response algorithm, whereas the response to neoadjuvant systemic therapy is usually evaluated using the modified Response Evaluation Criteria In Solid Tumors.

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

A. CT abdomen with IV contrast

According to the LI-RADS posttreatment response algorithm, an observation can be scored as "nonevaluable" in the setting of omission of multiphase imaging [17].

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

B. CT abdomen with IV contrast multiphase

Patients postablation are at a high risk for recurrence, and surveillance should be performed with contrast-enhanced CT or MRI every 3 to 6 months [4]. The National Comprehensive Cancer Network (NCCN) guidelines recommend follow-up imaging after locoregional therapy with CT or MRI every 3 to 6 months for 2 years, and every 6 to 12 months thereafter [24].

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

C. CT abdomen without and with IV contrast

The addition of a noncontrast series can assist in the evaluation for enhancement following some liver-directed therapies. This is especially true in the setting of postprocedural hemorrhage and in the setting of TACE using lipiodol, which is hyperdense on CT.

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

D. CT abdomen without IV contrast

Difficulties evaluating for potential underlying masses without the use of IV contrast limit the usefulness of noncontrast CT in screening for HCC. The current reference standard for monitoring treatment response is with contrast-enhanced CT or MRI [7].

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

E. FDG-PET/CT skull base to mid-thigh

There is no relevant literature supporting the use of FDG-PET in the setting of follow-up after liver-directed therapy.

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

F. MRI abdomen without and with IV contrast

Patients postablation are at a high risk for recurrence, and surveillance should be performed with

contrast-enhanced CT or MRI every 3 to 6 months [4]. The NCCN guidelines recommend follow-up imaging after resection, transplant, or locoregional therapy with CT or MRI every 3 to 6 months for 2 years, and every 6 to 12 months thereafter [24].

MRI may be preferable to CT after iodized oil-TACE because high-density oil within an embolized tumor may obscure residual or recurrent enhancement [25].

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

G. MRI abdomen without and with IV contrast with MRCP

There is a lack of evidence for the addition of MRCP sequences to an MR abdomen without and with IV contrast in follow-up after liver-directed therapy. In patients with a history of biliary disease, clinicians may elect to add an MRCP sequence.

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

H. MRI abdomen without IV contrast

Difficulties evaluating for potential underlying masses without the use of IV contrast limit the usefulness of noncontrast MRI in the posttreatment evaluation after liver-directed therapy or neoadjuvant chemotherapy. Current reference standard for monitoring treatment response is with contrast-enhanced MRI or CT [7].

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

I. MRI abdomen without IV contrast with MRCP

There is a lack of evidence for the addition of MRCP sequences to an MR abdomen without IV contrast in follow-up after liver-directed therapy.

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

J. US abdomen transabdominal

There is no relevant literature to support the role of transabdominal US in follow-up after liver-directed therapy.

Variant 4: Adult. Primary liver cancer. Posttreatment evaluation after liver directed therapy or neoadjuvant chemotherapy.

K. US abdomen with IV contrast

An alternative to contrast-enhanced CT or MRI, CEUS can be used to evaluate treatment response and assess for viable HCC. A CEUS LI-RADS treatment response algorithm has been released in 2024 [26]. However, CEUS is limited for certain patients because only 1 or 2 lesions can be evaluated during the examination, and there may be incomplete visualization of the entire liver.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

Surgical treatment for HCC is accepted as the most curative treatment. This includes both hepatic resection and liver transplantation. These treatments yield the best outcomes, with 5-year survivals averaging approximately 70% to 80% [27]. Recurrence rates after resection alone can be as high as 70% at 5 years; these can occur early (<2 years) most likely secondary to micrometastases or late (>2 years), likely a result of the development of a separate de novo HCC [6]. The recurrence rates following transplant are approximately 10% to 15% at 5 years [6]. The use of "bridging therapies"

as mentioned previously has been shown to reduce transplant list dropout as well as posttransplant recurrence [28].

The decision for the patient to undergo surgical resection versus transplantation is a complex multidisciplinary decision that is beyond the scope of these guidelines. Because of the recurrence rates with both surgical options, patients undergo postresection and posttransplant imaging surveillance to identify any potentially recurrent disease early.

This variant also includes patients who have undergone liver-directed therapy and have completed the immediate period of close follow-up imaging, with lesions being effectively treated fully and who are now ready to return to routine surveillance.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

A. CT abdomen with IV contrast

Because of HCCs' imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal, whereas single-phase CT does not allow for adequate lesion detection or characterization.

Both LI-RADS and OPTN provide technical recommendations for dynamic contrast-enhanced CT and MRI [19].

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

B. CT abdomen with IV contrast multiphase

The NCCN guidelines recommend routine surveillance after resection, transplant, or locoregional therapy with CT or MRI every 3 to 6 months for 2 years, and every 6 to 12 months thereafter [24]. Because of HCCs' imaging characteristics, cross-sectional imaging with multiple postcontrast phases is ideal.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

C. CT abdomen without and with IV contrast

There is a lack of evidence for the addition of a noncontrast phase to a contrast-enhanced CT in the setting of routine surveillance after liver-directed therapy, resection, or transplant. However, a noncontrast sequence can be of benefit to evaluate for the presence of postcontrast enhancement, especially in the setting of prior wedge resection with hyperdense surgical material, or prior TACE with the utilization of lipiodol.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

D. CT abdomen without IV contrast

Difficulties evaluating for potential underlying masses without the use of IV contrast limit the usefulness of noncontrast CT in routine surveillance of treated HCC.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

E. FDG-PET/CT skull base to mid-thigh

There is a lack of evidence for FDG-PET/CT and its usefulness in the routine surveillance of treated HCC.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

F. MRI abdomen without and with IV contrast

The NCCN guidelines recommend follow-up imaging after resection, transplant, or locoregional

therapy with CT or MRI every 3 to 6 months for 2 years, and every 6 to 12 months thereafter [24].

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

G. MRI abdomen without and with IV contrast with MRCP

There is a lack of evidence for the addition of MRCP sequences to an MRI abdomen without and with IV contrast in the routine surveillance of treated HCC. In patients with a history of biliary disease, clinicians may elect to add an MRCP sequence.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

H. MRI abdomen without IV contrast

Difficulties evaluating for potential underlying masses without the use of IV contrast limit the usefulness of noncontrast MRI in the routine surveillance of treated HCC. Both LI-RADS and OPTN provide technical recommendations for dynamic contrast-enhanced CT and MRI [19].

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

I. MRI abdomen without IV contrast with MRCP

There is a lack of evidence for the addition of MRCP sequences to an MRI abdomen without IV contrast in routine surveillance of treated HCC.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

J. US abdomen transabdominal

There is no relevant literature to support the use of US transabdominal in this clinical scenario.

Variant 5: Adult. Primary liver cancer. Treated. Routine surveillance.

K. US abdomen with IV contrast

There is no relevant literature to support the use of US abdomen with IV contrast in this clinical scenario.

Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- **Variant 1:** For screening patients at an increased risk of primary liver cancer, US abdomen is the recommended study. In certain patients, MRI abdomen either without and with IV contrast or without IV contrast, as well as CT abdomen with IV contrast multiphase may be appropriate. This is generally in the setting of poor-quality US, either due to body habitus or hepatic steatosis.
- **Variant 2:** In patients with known primary liver cancer presenting for staging, MRI abdomen without and with IV contrast or alternatively, CT abdomen with IV contrast multiphase are the recommended examinations for complete evaluation of the extent of the primary liver lesion(s), vascular involvement, and abdominal extrahepatic metastatic disease. The inclusion of an MRCP sequence may be appropriate, if there is concern for biliary involvement or in the setting of known primary sclerosing cholangitis or primary biliary cholangitis. A bone scan whole body may be appropriate, if there are suspicious osseous lesions. A CT pelvis with IV contrast may be of benefit for complete staging purposes. There was panel disagreement on the appropriateness of CT chest with IV contrast or CT chest without IV contrast; a chest CT is usually needed for complete staging purposes, and the disagreement between use of IV contrast is likely due to institutional differences.

- **Variant 3:** If there are known liver lesions undergoing active surveillance (LI-RADS 3 or 4 lesions), MRI abdomen without and with IV contrast or alternatively, CT abdomen with IV contrast multiphase are the recommended modalities for short-term follow-up of these lesions. The addition of an MRCP sequence may be appropriate, usually if there is concern for biliary pathology or involvement. In the setting of a multiphase CT, the addition of a noncontrast may be appropriate.
- **Variant 4:** In patients who have undergone liver-directed therapy or neoadjuvant chemotherapy, MRI abdomen without and with IV contrast, or CT abdomen with IV contrast multiphase, or CT abdomen without and with IV contrast are alternatives recommended for the evaluation of treatment response. The addition of the noncontrast phase for CT is most beneficial in the setting of liver-directed therapy. The addition of an MRCP sequence may be appropriate in the setting of biliary involvement or known pathology.
- **Variant 5:** After a patient has completed treatment for primary liver cancer, either remote liver-directed therapy or after liver transplant, and is undergoing surveillance, MRI abdomen without and with IV contrast or alternatively, CT abdomen with IV contrast multiphase are recommended. The addition of an MRCP sequence may be of benefit in the setting of biliary involvement or known pathology. For CT, the addition of a noncontrast series may be appropriate in the setting of prior liver-directed therapy.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at <https://acsearch.acr.org/list>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at <https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria>.

Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates the use of the current understanding of language inclusive of diversity in sex, intersex, gender, and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit

		ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
0	0 mSv	0 mSv
● (radioactive symbol)	<0.1 mSv	<0.03 mSv
● (radioactive symbol) ● (radioactive symbol)	0.1-1 mSv	0.03-0.3 mSv
● (radioactive symbol) ● (radioactive symbol) ● (radioactive symbol)	1-10 mSv	0.3-3 mSv
● (radioactive symbol) ● (radioactive symbol) ● (radioactive symbol) ● (radioactive symbol)	10-30 mSv	3-10 mSv
● (radioactive symbol)	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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Disclaimer

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may

influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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