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American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Suspected Liver Metastases**

Variant 1: **Initial imaging test following detection of primary tumor.**

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen in PVP	8		High
CT abdomen in HAP and PVP	8	HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	High
CT abdomen without contrast followed by HAP and PVP	6	HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	High
FDG-PET abdomen	6		High
MRI abdomen without and with contrast	6		None
MRI abdomen without contrast	5		None
MRI abdomen with reticulo-endothelial contrast	5		None
NUC liver scan with reticulo-endothelial agent	4		Med
US abdomen color Doppler	4		None
CT abdomen without contrast	4		Med
US abdomen	4		None
NUC immunoscintigraphy	3		IP
CTAP or CTA abdomen	2		Med
INV angiography liver	2		IP
NUC liver scan with blood pool agent	2		Med
NUC somatostatin receptor scintigraphy	2		High
Rating Scale: **1=Least appropriate, 9=Most appropriate**			***Relative Radiation Level**

Clinical Condition: **Suspected Liver Metastases**

Variant 2: **Surveillance following treatment of primary tumor.**

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen in PVP	8		High
CT abdomen without contrast followed by HAP and PVP	8	HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	High
CT abdomen in HAP and PVP	8	HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	High
MRI abdomen without and with contrast	6		None
FDG-PET abdomen	6		High
MRI abdomen with reticulo-endothelial contrast	5		None
MRI abdomen without contrast	4		None
US abdomen color Doppler	4		None
CT abdomen without contrast	4		Med
NUC immunoscintigraphy	4		IP
US abdomen	4		None
NUC somatostatin receptor scintigraphy	4		High
NUC liver scan with reticulo-endothelial agent	4		Med
CTAP or CTA abdomen	2		Med
NUC liver scan with blood pool agent	2		Med
US abdomen intraoperative / laparoscopic	2		None
INV angiography liver	2		IP
Rating Scale: **1=Least appropriate, 9=Most appropriate**			***Relative Radiation Level**

Clinical Condition: **Suspected Liver Metastases**

Variant 3: **Abnormal surveillance US, CT, or MRI, in PVP: high suspicion of malignancy.**

Radiologic Procedure	Rating	Comments	RRL*
INV image-guided biopsy liver	8		IP
CT abdomen in HAP and PVP	8	HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	High
FDG-PET abdomen	7		High
MRI abdomen without and with contrast	7		None
US abdomen intraoperative / laparoscopic	4		None
MRI abdomen without contrast	4		None
US abdomen	4		None
US abdomen color Doppler	4		None
MRI abdomen with reticulo-endothelial contrast	4		None
CT abdomen without contrast followed by HAP and PVP	4	HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	High
CTAP or CTA abdomen	3		Med
NUC immunoscintigraphy	3		IP
NUC liver scan with blood pool agent	3		Med
INV angiography liver	3		IP
NUC somatostatin receptor scintigraphy	3		High
NUC liver scan with reticulo-endothelial agent	3		Med
CT abdomen without contrast	2		Med
Rating Scale: **1=Least appropriate, 9=Most appropriate**			***Relative Radiation Level**

Clinical Condition: **Suspected Liver Metastases**

Variant 4: **Abnormal surveillance US, CT, or MRI in PVP: high suspicion of benignancy.**

Radiologic Procedure	Rating	Comments	RRL*
MRI abdomen without and with contrast	8		None
CT abdomen in HAP and PVP	7		High
CT abdomen without contrast followed by HAP and PVP	5		High
MRI abdomen without contrast	5		None
US abdomen	4		None
NUC liver scan with blood pool agent	4	May be indicated with large lesion with high suspicion of hemangioma.	Med
MRI abdomen with reticulo-endothelial contrast	4		None
INV image-guided biopsy liver	4		IP
NUC liver scan with reticulo-endothelial agent	4		Med
US abdomen color Doppler	4		None
NUC somatostatin receptor scintigraphy	3		High
US abdomen intraoperative / laparoscopic	3		None
CTAP or CTA abdomen	3		Med
FDG-PET abdomen	2		High
CT abdomen without contrast	2		Med
NUC immunoscintigraphy	2		IP
INV angiography liver	2		IP
Rating Scale: **1=Least appropriate, 9=Most appropriate**			***Relative Radiation Level**

Expert Panel on Gastrointestinal Imaging: Jay P. Heiken, MD[1]; Robert L. Bree, MD, MHSA[2]; W. Dennis Foley, MD[3]; Spencer B. Gay, MD[4]; Seth N. Glick, MD[5]; James E. Huprich, MD[6]; Marc S. Levine, MD[7]; Pablo R. Ros, MD, MPH[8]; Max Paul Rosen, MD, MPH[9]; William P. Shuman, MD[10]; Frederick L. Greene, MD.[11]

Summary of Literature Review

In the United States, metastatic disease is the most common cause of malignancy in the liver and is 20 to 50 times more common than primary liver cancer. The colon, stomach, pancreas, and breast are the most common primary sites. The appearance of a new lesion in the liver in a patient with a history of cancer strongly suggests hepatic metastasis. On the other hand, most small (1-1.5 cm) liver lesions, even in patients with known malignancy, are not malignant, especially if there are fewer than five lesions [1,2]. In most series, about one-third of patients who die with a malignancy have liver involvement.

The liver is susceptible to metastatic disease primarily due to the nature of the endothelial lining. The dual blood supply to the liver has an effect on the vascularity of liver metastases, with those supplied by the hepatic arterial system being more vascular than those supplied by the portal venous system. Most gastrointestinal cancer is spread through the portal venous system, whereas other tumors are spread through the hepatic arterial system [3]. Numerous imaging methods are available for detecting intrahepatic metastatic disease before, during, and after definitive therapy for the primary lesion. The usefulness of various imaging modalities can vary significantly across institutions because of local radiological expertise, availability of equipment or personnel, and the wishes and biases of treating physicians and radiologists.

This review will attempt to identify the broad variety of available imaging tests so that each can be rated by the consensus panel, realizing that many published scientific studies do not compare all imaging modalities at the current state of the art [4,5].

Ultrasound

Ultrasound (US) is the most available technique for liver imaging worldwide, and in many countries is the major modality used to search for liver metastases. In the United States, the relative availability of computed tomography (CT) and magnetic resonance imaging (MRI) and limited physician involvement in the performance of US, contribute to a lesser role for US diagnosis. Many patients have liver masses detected by US when suspicion of metastases is not high. In general, in the United States pretreatment and post-treatment screening for metastases is performed less often with US. Comparative studies demonstrate that US has high specificity but lower sensitivity than other imaging modalities [4-6]. With US, metastases can be hypoechoic, hyperechoic, cystic, or diffuse. Doppler may be useful, particularly in vascular lesions such as neuroendocrine tumors, sarcomas and lymphomas. Metastases frequently displace normal liver vessels.

Intraoperative/Laparoscopic Ultrasound

Intraoperative ultrasound (IOUS) is the most accurate imaging technique for detecting liver metastases at the time of primary tumor resection or resection of known metastases. It is complementary to surgical inspection and palpation. Additionally, intraoperative US can be important for localization of tumors for ablative techniques or to guide intraoperative biopsy or surgical resection [4,5,7,8]. Laparoscopic US (LUS) has been developed as an alternative to open intraoperative US with promising results. In one study of 55 patients with primary and secondary liver neoplasms who underwent LUS as part of a tumor ablation procedure, LUS demonstrated all 201 liver tumors shown by triphasic CT and an additional 21 lesions not shown by CT [9].

Computed Tomography

CT is particularly suited for the evaluation of metastatic disease, because the liver and potential extra-hepatic sites of tumor spread can be evaluated during the same examination. Helical CT is the preferred examination in the United States for surveillance for metastatic disease after treatment of the primary neoplasm, with multidetector CT representing the current state of the art. Because most hepatic metastases are relatively hypovascular compared with normal liver parenchyma, the lesions are hypoattenuating when imaged during the peak of hepatic parenchymal enhancement (portal venous phase). In general, therefore, imaging during the portal venous phase of hepatic enhancement is adequate to detect most hepatic lesions in most patients [10-12].

Hypervascular lesions are less common, and tumors in this group include metastases from renal cell carcinoma,

[1]Review Author, Mallinckrodt Institute of Radiology, St. Louis, Mo; [2]Panel Chair, Radia Medical Imaging, Everett, Wash; [3]Froedtert Hospital East, Milwaukee, Wis; [4]University of Virginia Health Science Center, Charlottesville, Va; [5]Presbyterian Medical Center, Philadelphia, Pa; [6] Mayo Clinic, Rochester, Minn; [7] Hospital of the University of Pennsylvania, Philadelphia, Pa; [8] Brigham & Women's Hospital, Boston, Mass; [9] Beth Israel Hospital, Boston, Mass; [10] University of Washington, Seattle, Wash; [11] Carolinas Medical Center, Charlotte, NC, American College of Surgeons.

Reprint requests to: Department of Quality & Safety, American College of Radiology, 1891 Preston White Drive, Reston, VA 20191-4397.

carcinoid, islet cell carcinoma, thyroid carcinoma, melanoma, and neuroendocrine tumors. In a large series of patients, small (<2 cm) hypervascular lesions were seen better in the arterial phase than in the portal venous phase [13]. With the widespread use of multidetector row scanners, arterial phase scanning can be routine. Although metastases from breast carcinoma are sometimes hypervascular, one study showed that arterial phase imaging was not necessary in this group [11]. Hypervascular lesions may be isoattenuating to liver during the portal venous phase of hepatic enhancement. With helical CT, both arterial and portal venous phase imaging is recommended for patients with hypervascular primary tumors. If helical CT is not available, a noncontrast scan can also be useful [14].

CT arterial portography is no longer used extensively, as it is an invasive angiographic technique that often yields confusing artifacts that decreases accuracy [4-6,12,14]. Newer arterial mapping techniques using MR and CT angiography have largely replaced standard angiographic techniques for preoperative staging.

When CT is used to characterize a liver lesion detected with US, the CT examination should include arterial phase and portal venous phase imaging Many incidentally discovered liver lesions are hypervascular and therefore may be demonstrated and/or characterized accurately only if arterial phase imaging is included [15,16].

Magnetic Resonance Imaging

With MRI, most hepatic metastases, like most liver lesions, are hypointense to normal liver on T1-weighted images and hyperintense to liver on T2-weighted images. Some morphologic features have been shown to be useful in distinguishing metastatic lesions from common benign lesions such as hemangiomas and cysts. Findings in metastatic disease include heterogenous signal intensity with an irregular or indistinct outer margin, smooth or irregular central areas of high signal intensity surrounded by a ring of low signal intensity, or a mass surrounded by a ring of high signal intensity. On T2-weighted images, hemangiomas are hyperintense compared with normal liver parenchyma and generally higher in signal intensity than metastases. The typical early enhancement pattern of hemangiomas after administration of gadolinium chelates is eccentric, nodular peripheral enhancement. When present, this pattern, which is similar to that seen with contrast enhanced CT, is highly accurate in distinguishing hemangiomas from metastases.

Several studies have compared the accuracy of various MR techniques to other standard imaging modalities. A large clinical trial in the Radiology Diagnostic Oncology Group (RDOG) series compared MR to CT in metastatic colorectal cancer to the liver. CT had a higher sensitivity and similar specificity as compared to MR [17]. Rapid imaging with breath holding has been found to be more sensitive for hepatic masses than conventional non-breath-hold spin-echo techniques [18].

There is continued debate about the value of MR contrast agents. One study showed gadolinium chelate-enhanced 3D rapid gradient echo imaging to be superior to unenhanced MR imaging for detecting focal hepatic masses [19]. Another study, however, demonstrated no statistically significant difference between unenhanced and gadolinium-enhanced MR imaging in differentiating patients with liver metastases from those without metastases [20]. Nevertheless, most experts in body MR imaging consider gadolinium chelate enhancement to be an essential part of the abdominal MR imaging examination of colorectal cancer patients being evaluated for possible liver metastases. A report in 51 patients suggests that MR with superparamagnetic iron oxide contrast (SPIO) may be slightly superior to dual-phase CT for patients with colorectal metastases [7].

Nuclear Imaging

Positron emission tomography (PET) has become more widely used in detecting metastatic disease. A meta-analysis comparing US, CT, MRI, and 18F fluorodeoxyglucose (FDG) PET in patients with cancers of the gastrointestinal tract concluded that FDG-PET is the most sensitive imaging test for the diagnosis of hepatic metastases from colorectal cancer [21]. In addition, several studies have demonstrated that the addition of FDG-PET to a conventional staging evaluation in colorectal cancer patients with potentially resectable liver metastases results in a change in management of 20%-32%, mainly due to detection of unknown extrahepatic disease [22-24]. PET also has been shown to be accurate in distinguishing benign from malignant liver tumors [25]. A limitation of FDG-PET, however, is that it may fail to demonstrate small (< 1 cm) liver metastases [22,26,27]. For staging and restaging patients with colorectal liver metastases, integration of CT and FDG-PET data, either by fusion or by integrated PET-CT imaging, enables better management guidance than with either technique alone [28].

Traditional reticulo-endothelial imaging or blood pool imaging can be useful for characterizing masses such as focal nodular hyperplasia or hemangioma but are not typically used for detecting metastatic disease. Newer agents such as isotope-tagged monoclonal antibodies directed toward surface proteins expressed by colorectal liver metastases have had some initial success in solving difficult clinical problems [4,5]. Liver metastases from endocrine active tumors from the pancreas or gastrointestinal tract can be detected by somatostatin receptor scintigraphy [5].

Summary

Many radiologic techniques are available for preoperative detection of liver metastases and postoperative surveillance. Some of the less widely used screening techniques can be useful when there is a need for specific problem solving. Rapid technological and clinical advances in equipment, contrast agents, and radioisotopes make direct comparison of the various techniques difficult. In addition, local custom and equipment availability within communities or medical centers can be expected to lead to a variety of indications and applications in detecting hepatic metastatic disease.

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