ACG Clinical Guideline: Diagnosis and Management of Focal Liver Lesions

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Abstract

Focal liver lesions (FLL) have been a common reason for consultation faced by gastroenterologists and hepatologists. The increasing and widespread use of imaging studies has led to an increase in detection of incidental FLL. It is important to consider not only malignant liver lesions, but also benign solid and cystic liver lesions such as hemangioma, focal nodular hyperplasia, hepatocellular adenoma, and hepatic cysts, in the differential diagnosis. In this ACG practice guideline, the authors provide an evidence-based approach to the diagnosis and management of FLL.

Preamble

The writing group was invited by the Practice Parameters Committee and the Board of the Trustees of the American College of Gastroenterology to develop a practice guideline regarding the suggested diagnostic approaches and management of focal liver lesions (FLLs). FLLs are solid or cystic masses or areas of tissue that are identified as an abnormal part of the liver. The term “lesion” rather than “mass” was chosen because “lesion” is a term that has a wider application, including solid and cystic masses. This guideline will be limited to primary liver lesions and the management approach to FLLs rather than focusing on the diagnosis and management of metastatic lesions, hepatocellular carcinoma, or cholangiocarcinoma. For specific reading on these lesions, the reader is referred to other recent guidelines (1–3). An evidence-based approach was undertaken to critically review the available diagnostic tests and treatment options of FLLs. The following resources were utilized: (i) a formal review and analysis of the published literature using MEDLINE via the OVID interface up to June 2013 with the search terms “hepatic/liver mass,” “hepatic/liver tumor,” “hepatic/liver cancer,” “hepatic/liver lesion,” “hepatocellular adenoma,” “liver adenomatosis,” “hepatic hemangioma,” “focal nodular hyperplasia,” “nodular regenerative hyperplasia,” “hepatic cyst,” “hepatic cystadenoma,” “hepatic cystadenocarcinoma,” “polycystic liver disease,” and “hydatid cyst,” without language restriction; (ii) hand reviews of articles known to the authors; and (iii) the consensus experiences of the authors and independent reviewers regarding FLLs. The guideline was prepared according to the policies of the American College of Gastroenterology and with the guidance of the Practice Parameters Committee. The GRADE system was used to grade the strength of recommendations and the quality of evidence (4).

Introduction

Because of the widespread clinical use of imaging modalities such as ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI), previously unsuspected liver lesions are increasingly being discovered in otherwise asymptomatic patients. A recent study indicated that from 1996 to 2010 the use of CT examinations tripled (52/1,000 patients in 1996 to 149/1,000 in 2010, 7.8% annual growth), MRIs quadrupled (17/1,000 to 65/1,000, 10% annual growth); US approximately doubled (134/1,000 to 230/1,000, 3.9% annual growth), and positron emission tomography (PET) scans increased from 0.24/1,000 patients to 3.6/1,000 patients (57% annual growth) (5). More importantly, the evaluation of liver lesions has taken on greater importance because of the increasing incidence of primary hepatic malignancies, especially hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA). Therefore, a thorough and systematic approach to the management of focal liver lesions (FLLs) is of utmost importance.

Table 1. Recommendations
The GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system for grading evidence and strength of recommendations
Strength of recommendations
Strong: the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not.
Weak: the tradeoffs are less certain between the desirable and undesirable effects of an intervention.
Quality of evidence
High: further research is very unlikely to change our confidence in the estimate of effect.
Moderate: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low: any estimate of effect is very uncertain.
Solid FLL
Suspected hepatocellular carcinoma
1. An MRI or triple-phase CT should be obtained in patients with cirrhosis with an ultrasound showing a lesion of > 1 cm (strong recommendation, moderate quality of evidence).
2. Patients with chronic liver disease, especially with cirrhosis, who present with a solid FLL are at a very high risk for having HCC and must be considered to have HCC until otherwise proven (strong recommendation, moderate quality of evidence).
3. A diagnosis of HCC can be made with CT or MRI if the typical characteristics are present: a solid FLL with enhancement in the arterial phase with washout in the delayed venous phase should be considered to have HCC until otherwise proven (strong recommendation, moderate quality of evidence).
4. If an FLL in a patient with cirrhosis does not have typical characteristics of HCC, then a biopsy should be performed in order to make the diagnosis (strong recommendation, moderate quality of evidence).

Table 1. Recommendations *continued*
Suspected cholangiocarcinoma
5. MRI or CT should be obtained if CCA is suspected clinically or by ultrasound (strong recommendation, low quality of evidence).
6. A liver biopsy should be obtained to establish the diagnosis of CCA if the patient is nonoperable (strong recommendation, low quality of evidence).
Suspected hepatocellular adenoma
7. Oral contraceptives, hormone-containing IUDs, and anabolic steroids are to be avoided in patients with hepatocellular adenoma (strong recommendation, moderate quality of evidence).
8. Obtaining a biopsy should be reserved for cases in which imaging is inconclusive and biopsy is deemed necessary to make treatment decisions (strong recommendation, low quality of evidence).
9. Pregnancy is not generally contraindicated in cases of hepatocellular adenoma < 5 cm and an individualized approach is advocated for these patients (conditional recommendation, low quality of evidence).
10. In hepatocellular adenoma ≥ 5 cm, intervention through surgical or nonsurgical modalities is recommended, as there is a risk of rupture and malignancy (conditional recommendation, low quality of evidence).
11. If no therapeutic intervention is pursued, lesions suspected of being hepatocellular adenoma require follow-up CT or MRI at 6- to 12-month intervals. The duration of monitoring is based on the growth patterns and stability of the lesion over time (conditional recommendation, low quality of evidence).
Suspected hemangioma
12. An MRI or CT scan should be obtained to confirm a diagnosis of hemangioma (strong recommendation, moderate quality of evidence).
13. Liver biopsy should be avoided if the radiologic features of a hemangioma are present (strong recommendation, low quality of evidence).
14. Pregnancy and the use of oral contraceptives or anabolic steroids are not contraindicated in patients with a hemangioma (conditional recommendation, low quality of evidence).
15. Regardless of the size, no intervention is required for asymptomatic hepatic hemangiomas. Symptomatic patients with impaired quality of life can be referred for surgical or nonsurgical therapeutic modalities by an experienced team (conditional recommendation, low quality of evidence).
Suspected focal nodular hyperplasia
16. An MRI or CT scan should be obtained to confirm a diagnosis of FNH. A liver biopsy is not routinely indicated to confirm the diagnosis (strong recommendation, low quality of evidence).
17. Pregnancy and the use of oral contraceptives or anabolic steroids are not contraindicated in patients with FNH (conditional recommendation, low quality of evidence).
18. Asymptomatic FNH does not require intervention (strong recommendation, moderate quality of evidence).
19. Annual US for 2 – 3 years is prudent in women diagnosed with FNH who wish to continue OCP use. Individuals with a firm diagnosis of FNH who are not using OCP do not require follow-up imaging (conditional recommendation, low quality of evidence).

Table 1. Recommendations *continued*
Suspected nodular regenerative hyperplasia
20. Liver biopsy is required to confirm the diagnosis of NRH (strong recommendation, moderate quality of evidence).
21. Pregnancy and the use of oral contraceptives or anabolic steroids are not contraindicated in patients with an NRH (conditional recommendation, low quality of evidence).
22. Asymptomatic NRH does not require intervention (conditional recommendation, low quality of evidence).
23. Management of NRH is based on diagnosing and managing any underlying predisposing disease processes (strong recommendation, low quality of evidence).
Cystic FLL
Suspect simple hepatic cysts
24. A hepatic cyst identified on US with septations, fenestrations, calcifications, irregular walls, or daughter cysts should prompt further evaluation with a CT or MRI (strong recommendation, low quality of evidence).
25. Asymptomatic simple hepatic cysts should be observed with expectant management (strong recommendation, moderate quality of evidence).
26. Aspiration of asymptomatic, simple hepatic cysts is not recommended (strong recommendation, low quality of evidence).
27. Symptomatic simple hepatic cysts may be managed with laparoscopic deroofing rather than aspiration and sclerotherapy, dictated based on availability of local expertise (conditional recommendation, low quality of evidence).
Suspected biliary cystadenoma or cystadenocarcinoma
28. Routine fluid aspiration is not recommended when BCA is suspected because of limited sensitivity and the risk of malignant dissemination (strong recommendation, low quality of evidence).
29. Imaging characteristics suggestive of BC or BCA, such as internal septations, fenestrations, calcifications, or irregular walls, should lead to referral for surgical excision (strong recommendation, low quality of evidence).
30. Complete surgical excision, by an experienced team, is recommended if BC or BCA is suspected (strong recommendation, low quality of evidence)
Suspected polycystic liver disease
31. Routine medical therapy with mammalian target of rapamycin inhibitors or somatostatin analogs is not recommended (strong recommendation, low quality of evidence).
32. Aspiration, deroofing, resection of a dominant cyst(s) can be performed based on the patient's clinical presentation and underlying hepatic reserve (conditional recommendation, low quality of evidence).
33. Liver transplantation with or without kidney transplantation can be considered in patients with refractory symptoms and significant cyst burden (conditional recommendation, low quality of evidence).

Table 1. Recommendations *continued*
Suspected hydatid cysts
34. MRI is preferred over CT for concomitant evaluation of the biliary tree and cystic contents (conditional recommendation, low quality of evidence).
35. Monotherapy with antihelminthic drugs is not recommended in symptomatic patients who are surgical or percutaneous treatment candidates (strong recommendation, moderate quality of evidence).
36. Adjunctive therapy with antihelminthic therapy is recommended in patients undergoing PAIR or surgery, and in those with peritoneal rupture or biliary rupture (strong recommendation, low quality of evidence).
37. Percutaneous treatment with PAIR is recommended for patients with active hydatid cysts who are not surgical candidates, who decline surgery, or who relapse after surgery (strong recommendation, low quality of evidence).
38. Surgery, either laparoscopic or open, based on available expertise, is recommended in complicated hydatid cysts with multiple vesicles, daughter cysts, fistulas, rupture, hemorrhage, or secondary infection (strong recommendation, low quality of evidence).
BC, biliary cystadenoma; BCA, biliary cystadenocarcinoma; CCA, cholangiocarcinoma; CT, computed tomography; FLL, focal liver lesion; FNH, focal nodular hyperplasia; HCC, hepatocellular carcinoma; IUD, intrauterine device; MRI, magnetic resonance imaging; NRH, nodular regenerative hyperplasia; OCP, oral contraceptive; PAIR, puncture, aspiration, injection, and reaspiration; US, ultrasonography.

Table 3. Imaging characteristics of solid liver lesions

Lesion	US	CT	MRI
HCA	Heterogeneous; hyperechoic if steatotic but anechoic center if hemorrhage	Well demarcated with peripheral enhancement; homogenous more often than heterogeneous; hypodense if steatotic, hyperdense if hemorrhagic	HNF1α: signal lost on chemical shift; moderate arterial enhancement without persistent enhancement during delayed phase IHCA: markedly hyperintense on T2 with stronger signal peripherally; persistent enhancement in delayed phase β-Catenin: inflammatory subtype has same appearance as IHCA; noninflammatory is heterogeneous with no signal dropout on chemical shift, isointense of T1 and T2 with strong arterial enhancement and delayed washout
THCA	Variable appearance	Hypo- to isoattenuating	T1: heterogeneous and well-defined iso- to hyperintense mass. Strongly hyperintense with persistent contrast enhancement in delayed phase
Hemangioma	Hyperechoic with well-defined rim and with few intranodular vessels	Discontinuous peripheral nodular enhancement isoattenuating to aorta with progressive centripetal fill-in	T1: hypointense; discontinuous peripheral enhancement with centripetal fill-in T2: hyperintense relative to spleen
FNH	Generally isoechoic	Central scar. Arterial phase shows homogenous hyperdense lesion; returns to precontrast density during portal phase that is hypo- or isodense	T1: isointense or slightly hypointense. Gadolinium produces early enhancement with central scar enhancement during delayed phase T2: slightly hyperintense or isointense
NRH	Isoechoic/hyperechoic	Nonenhancing nodules, some- times hypodense, with variable sizes (most sub-centimeter)	T1: hyperintense T2: varied intensity (hypo/iso/hyperintense)

CT, computed tomography; FNH, focal nodular hyperplasia; HCA, hepatocellular adenoma; HNF1α, hepatocyte nuclear factor-1α; IHCA, inflammatory hepatocellular adenoma; MRI, magnetic resonance imaging; NRH, nodular regenerative hyperplasia; THCA, telangiectatic hepatocellular adenoma; US, ultrasonography.
Adapted from Shaked *et al*. (52).

Table 4. Imaging characteristics of cystic liver lesions			
Lesion	**US**	**CT**	**MRI**
Simple hepatic cysts (SHCs)	Anechoic, homogeneous, fluid filled. Smooth margins	Well-demarcated, water-attenuated, smooth lesion without an internal structure. No enhancement with contrast	Well-defined, homogeneous lesion. No enhancement with contrast. T1: hypointense signal intensity T2: hyperintense signal intensity
Biliary cystadenomas (BCs)	Irregular walls, internal septations forming loculi	Heterogeneous septations, internal septations, irregular papillary growths, thickened cyst walls	May appear heterogeneous. T1: Hypointense signal intensity T2: Hyperintense signal intensity
Polycystic liver disease (PCLD)	Multiple hepatic cysts, similar in characteristics to SHC US findings	Multiple hepatic cysts, similar in characteristics to SHC CT findings	Multiple hepatic cysts, similar in characteristics to SHC MRI findings
Hydatid cysts (HCs)	May appear similar to SHC. Progress to develop thick, calcified walls, hyperechoic/ hypoechoic contents. Daughter cysts in periphery.	Hypodense lesion with hypervascular pericyst wall, distinct endocyst wall. Calcified walls and septa easily detect- ed. Daughter cysts seen peripherally within mother cyst.	T1: Hypointense signal intensity of cyst contents. T2: Hyperintense signal intensity of cyst contents. Hypointense rim on T2. Daughter cysts seen peripherally within mother cyst. Collapse parasitic membranes seen as floating linear structures within cyst.
CT, computed tomography; MRI, magnetic resonance imaging; US, ultrasonography.			

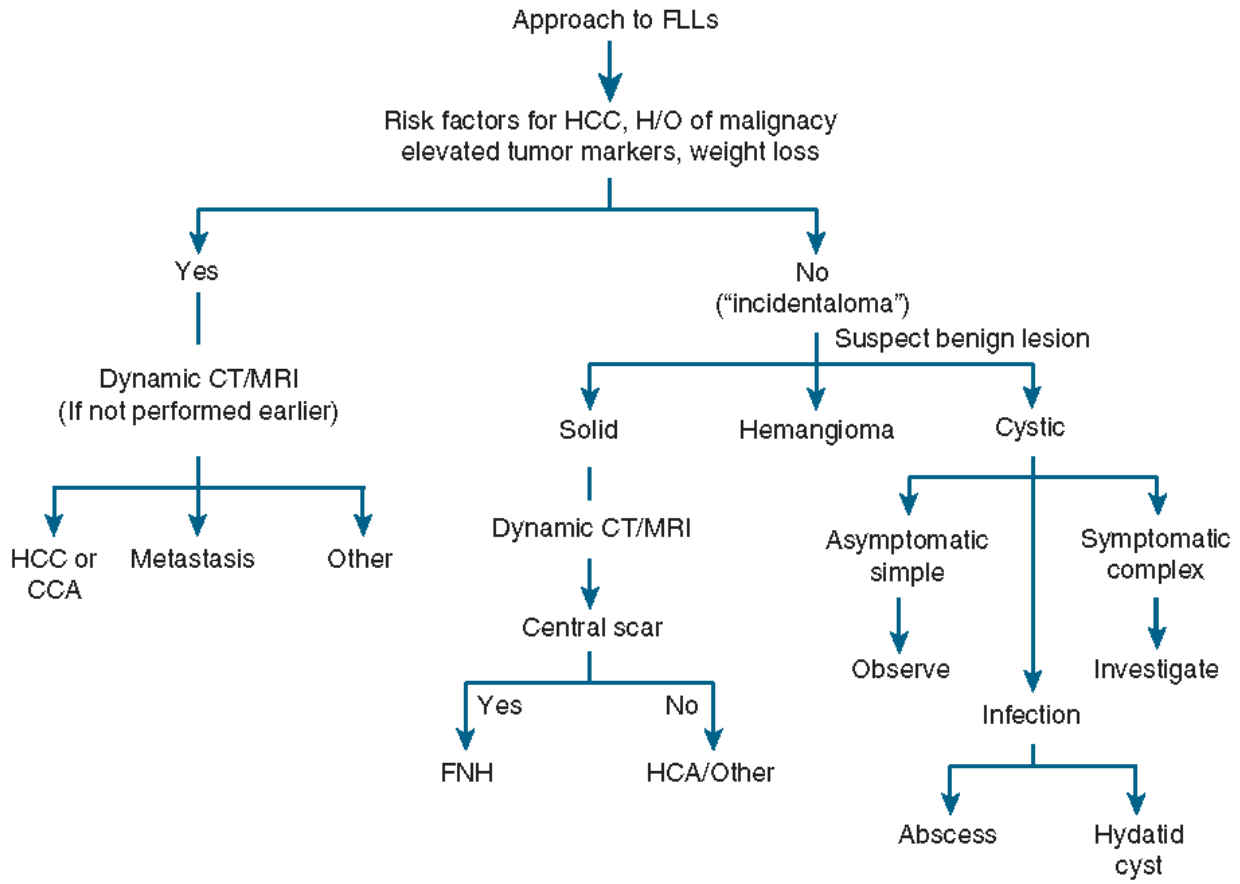

Figure 1 . Approach to FLLs. CCA, cholangiocarcinoma; CT, computed tomography; FLL, focal liver lesion; FNH, focal nodular hyperplasia; HCA, hepatocellular adenoma; HCC, hepatocellular carcinoma; H / O, history of; MRI, magnetic resonance imaging .