

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Asrani SK, Larson JJ, Yawn B, Therneau TM, Kim WR. Underestimation of liver-related mortality in the United States. <i>Gastroenterology</i> . 2013;145(2):375-382 e371-372.	Review/Other-Dx	261 patients	To update data on liver mortality in the United States.	The Rochester Epidemiology Project database contained information on 261 liver-related deaths, with an age- and sex-adjusted death rate of 27.0/100,000 persons (95% confidence interval: 23.7-30.3). Of these, only 71 deaths (27.2%) would have been captured by the NCHS definition. Of cases for which viral hepatitis or hepatobiliary cancer was the cause of death, 96.9% and 94.3% had liver-related immediate causes of death, respectively. In analysis of data from the National Death registry (2008), use of the updated definition increased liver mortality by >2-fold (from 11.7 to 25.7 deaths/100,000, respectively). Using NCHS definitions, liver-related deaths decreased from 18.9/100,000 in 1979 to 11.7/100,000 in 2008—a reduction of 38%. However, using the updated estimate, liver-related deaths were essentially unchanged from 1979 (25.8/100,000) to 2008 (25.7/100,000). Mortality burden was systematically underestimated among non-whites and persons of Hispanic ethnicity.	4
2. Udompap P, Kim D, Kim WR. Current and Future Burden of Chronic Nonmalignant Liver Disease. <i>Clin Gastroenterol Hepatol</i> . 2015;13(12):2031-2041.	Review/Other-Dx	N/A	To assemble available data on the burden of CLD in the United States	The overall burden, including mortality, associated with CLD has increased in the United States. On the basis of available epidemiologic data, viral hepatitis, ALD, and NAFLD are the most common etiologies for CLD.	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
3. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. <i>Ann Intern Med.</i> 2006;144(10):705-714.	Review/Other-Dx	N/A	To describe the HCV-infected population in the United States.	The prevalence of anti-HCV in the United States was 1.6% (95% CI, 1.3% to 1.9%), equating to an estimated 4.1 million (CI, 3.4 million to 4.9 million) anti-HCV-positive persons nationwide; 1.3% or 3.2 million (CI, 2.7 million to 3.9 million) persons had chronic HCV infection. Peak prevalence of anti-HCV (4.3%) was observed among persons 40 to 49 years of age. A total of 48.4% of anti-HCV-positive persons between 20 and 59 years of age reported a history of injection drug use, the strongest risk factor for HCV infection. Of all persons reporting such a history, 83.3% had not used injection drugs for at least 1 year before the survey. Other significant risk factors included 20 or more lifetime sex partners and blood transfusion before 1992. Abnormal serum ALT levels were found in 58.7% of HCV RNA-positive persons. Three characteristics (abnormal serum ALT level, any history of injection drug use, and history of blood transfusion before 1992) identified 85.1% of HCV RNA-positive participants between 20 and 59 years of age.	4
4. Davis GL, Alter MJ, El-Serag H, Poynard T, Jennings LW. Aging of hepatitis C virus (HCV)-infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression. <i>Gastroenterology.</i> 2010;138(2):513-521, 521 e511-516.	Review/Other-Dx	N/A	To project the future prevalence of CH-C and its complications.	Prevalence of CH-C peaked in 2001 at 3.6 million. Fibrosis progression was inversely related to age at infection, so cirrhosis and its complications were most common after the age of 60 years, regardless of when infection occurred. The proportion of CH-C with cirrhosis is projected to reach 25% in 2010 and 45% in 2030, although the total number with cirrhosis will peak at 1.0 million (30.5% higher than the current level) in 2020 and then decline. Hepatic decompensation and liver cancer will continue to increase for another 10 to 13 years. Treatment of all infected patients in 2010 could reduce risk of cirrhosis, decompensation, cancer, and liver-related deaths by 16%, 42%, 31%, and 36% by 2020, given current response rates to antiviral therapy.	4

* See Last Page for Key

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
5. Morgan RL, Baack B, Smith BD, Yartel A, Pitasi M, Falck-Ytter Y. Eradication of hepatitis C virus infection and the development of hepatocellular carcinoma: a meta-analysis of observational studies. <i>Ann Intern Med.</i> 2013;158(5 Pt 1):329-337.	Meta-analysis	30 studies	To systematically review observational studies to determine the association between response to HCV therapy and development of HCC among persons at any stage of fibrosis and those with advanced liver disease.	Sustained virologic response after treatment among HCV-infected persons at any stage of fibrosis is associated with reduced HCC. The evidence was determined to be of moderate quality.	M
6. Lazo M, Hernaez R, Eberhardt MS, et al. Prevalence of nonalcoholic fatty liver disease in the United States: the Third National Health and Nutrition Examination Survey, 1988-1994. <i>Am J Epidemiol.</i> 2013;178(1):38-45.	Review/Other-Dx	12,454 adults	To use ultrasonography data to (1) estimate the prevalence of any hepatic steatosis and NAFLD in the United States by key sociodemographic characteristics and (2) to examine metabolic, anthropometric, and laboratory correlates of hepatic steatosis and NAFLD.	In the US population, the rates of prevalence of hepatic steatosis and NAFLD were 21.4% and 19.0%, respectively, corresponding to estimates of 32.5 (95% confidence interval: 29.9, 35.0) million adults with hepatic steatosis and 28.8 (95% confidence interval: 26.6, 31.2) million adults with NAFLD nationwide. After adjustment for age, income, education, body mass index (weight (kg)/height (m)(2)), and diabetes status, NAFLD was more common in Mexican Americans (24.1%) compared with non-Hispanic whites (17.8%) and non-Hispanic blacks (13.5%) (P = 0.001) and in men (20.2%) compared with women (15.8%) (P < 0.001). Hepatic steatosis and NAFLD were also independently associated with diabetes, with insulin resistance among people without diabetes, with dyslipidemia, and with obesity.	4
7. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD. Liver biopsy. <i>Hepatology.</i> 2009;49(3):1017-1044.	Review/Other-Dx	N/A	to summarize the current practice of liver biopsy and make recommendations about its performance.	No results stated in abstract.	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
8. Ratziu V, Charlotte F, Heurtier A, et al. Sampling variability of liver biopsy in nonalcoholic fatty liver disease. <i>Gastroenterology</i> . 2005;128(7):1898-1906.	Observational-Dx	51 patients with nonalcoholic fatty liver disease (NAFLD); each received 2 liver biopsies.	To assess the sampling error of liver biopsy and its impact on the diagnosis and staging of NASH.	No features displayed high agreement; substantial agreement was only seen for steatosis grade; moderate agreement for hepatocyte ballooning and perisinusoidal fibrosis; fair agreement for Mallory bodies; acidophilic bodies and lobular inflammation displayed only slight agreement. Overall, the discordance rate for the presence of hepatocyte ballooning was 18%, and ballooning would have been missed in 24% of patients had only 1 biopsy been performed. The negative predictive value of a single biopsy for the diagnosis of NASH was at best 0.74. Discordance of 1 stage or more was 41%. Six of 17 patients with bridging fibrosis (35%) on 1 sample had only mild or no fibrosis on the other and therefore could have been under staged with only 1 biopsy. Intraobserver variability was systematically lower than sampling variability and therefore could not account for most of the sampling error.	2
9. Regev A, Berho M, Jeffers LJ, et al. Sampling error and intraobserver variation in liver biopsy in patients with chronic HCV infection. <i>Am J Gastroenterol</i> . 2002;97(10):2614-2618.	Observational-Dx	124 patients	To determine the rate and extent of sampling error in patients with chronic hepatitis C virus infection, and to assess the intraobserver variation with the commonly used scoring system proposed by Scheuer and modified by Batts and Ludwig.	Thirty of 124 patients (24.2%) had a difference of at least one grade, and 41 of 124 patients (33.1%) had a difference of at least one stage between the right and left lobes. In 18 patients (14.5%), interpretation of cirrhosis was given in one lobe, whereas stage 3 fibrosis was given in the other. A difference of two stages or two grades was found in only three (2.4%) and two (1.6%) patients, respectively. Of the 50 samples that were examined twice, the grading by each pathologist on the second examination differed from the first examination in 0% and 4%, and the staging differed in 6% and 10%, respectively. All observed variations were of one grade or one stage.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
10. Asrani SK. Incorporation of Noninvasive Measures of Liver Fibrosis Into Clinical Practice: Diagnosis and Prognosis. Clin Gastroenterol Hepatol. 2015;13(12):2190-2204.	Review/Other-Dx	N/A	To review and (1) describe commonly available serum markers and elastography-based techniques, (2) discuss their role in diagnosis of liver fibrosis, (3) outline the advantages and limitations of the various techniques, and finally (4) describe the evolving prognostic role of noninvasive markers.	No results stated in abstract.	4
11. Parkes J, Guha IN, Roderick P, Rosenberg W. Performance of serum marker panels for liver fibrosis in chronic hepatitis C. J Hepatol. 2006;44(3):462-474.	Meta-analysis	14 studies	To assess the performance of panels of serum markers of hepatic fibrosis in CHC, incorporating analyses placing markers in a clinical context.	14 studies were included with 10 different panels. Median AUC in validation populations was 0.77 and training populations 0.81. Likelihood ratios (LR) ranged from -LR 0.1 to 0.9, + LR 1.2 to 33.1, diagnostic odds ratios (DOR) were 9.0 (median) with a range of 5 to 27- mostly below values of robust tests. Tests perform with either high sensitivity with low specificity or vice versa. Cut-off levels that gave clinically relevant predictive values for the presence/absence of significant fibrosis were applicable to 35% of the population.	M
12. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. Hepatology. 2011;53(3):1020-1022.	Review/Other-Tx	N/A	An update of the AASLD practice guidelines on the management of HCC which published in 2005.	n/a	4
13. El-Serag HB. Epidemiology of viral hepatitis and hepatocellular carcinoma. Gastroenterology. 2012;142(6):1264-1273 e1261.	Review/Other-Dx	N/A	To summarize the risk factors for HCC among HBV- or HCV-infected individuals, based on findings from epidemiologic studies and meta-analyses, as well as determinants of patient outcome and the HCC disease burden, globally and in the United States.	Most cases of hepatocellular carcinoma (HCC) are associated with cirrhosis related to chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection. Changes in the time trends of HCC and most variations in its age-, sex-, and race-specific rates among different regions are likely to be related to differences in hepatitis viruses that are most prevalent in a population, the timing of their spread, and the ages of the individuals the viruses infect. Environmental, host genetic, and viral factors can affect the risk of HCC in individuals with HBV or HCV infection.	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
14. Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975 to 2005. <i>J Clin Oncol.</i> 2009;27(9):1485-1491.	Review/Other-Dx	N/A	To monitor changes in the burden of Hepatocellular carcinoma (HCC) in the United States.	Age-adjusted HCC incidence rates tripled between 1975 and 2005. Incidence rates increased in each 10-year birth cohort from 1900 through the 1950s. Asians/Pacific Islanders had higher incidence and mortality rates than other racial/ethnic groups, but experienced a significant decrease in mortality rates over time. From 2000 to 2005, marked increases in incidence rates occurred among Hispanic, black, and white middle-aged men. Between 1992 and 2004, 2- to 4-year HCC survival rates doubled, as more patients were diagnosed with localized and regional HCC and prognosis improved, particularly for patients with reported treatment. Recent 1-year survival rates remained, however, less than 50%.	4
15. El-Serag HB. Hepatocellular carcinoma. <i>N Engl J Med.</i> 2011;365(12):1118-1127.	Review/Other-Tx	N/A	To review and summarize recent advances in prevention, surveillance, diagnosis, and treatment.	No results stated in abstract.	4
16. White DL, Kanwal F, El-Serag HB. Association between nonalcoholic fatty liver disease and risk for hepatocellular cancer, based on systematic review. <i>Clin Gastroenterol Hepatol.</i> 2012;10(12):1342-1359 e1342.	Review/Other-Dx	17 studies	To confirm the association between nonalcoholic fatty liver disease and hepatocellular carcinoma.	NAFLD or NASH cohorts with few or no cases of cirrhosis had a minimal risk for HCC (cumulative HCC mortality of 0%-3% for study periods up to 20 y). Cohorts with NASH and cirrhosis had a consistently higher risk (cumulative incidence ranging from 2.4% over 7 y to 12.8% over 3 y). However, the risk for HCC was substantially lower in these cohorts than for cohorts with hepatitis C-related cirrhosis. Factors that increased risk among cohorts with NASH and cirrhosis could not be determined, because most studies were not sufficiently powered for multivariate analysis.	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
17. Di Lelio A, Cestari C, Lomazzi A, Beretta L. Cirrhosis: diagnosis with sonographic study of the liver surface. Radiology. 1989;172(2):389-392.	Observational-Dx	50 healthy subjects, 75 patients with suspected diffuse chronic liver disease, and 225 patients with cancer.	To find an objective sonographic sign of cirrhosis.	A diagnosis of cirrhosis was made with sonography when surface irregularities were observed that were comparable to the anatomic abnormalities of a cirrhotic liver surface. An examination of the liver surface gave the best diagnostic rate for cirrhosis (88%). There were seven false-negative results, but in five of them no surface nodularity could be seen at laparoscopy, and the diagnosis was made only on the basis of histologic studies; there was one false-positive result. This study indicated that ultrasonography might be a reliable method to follow up patients with chronic liver disease that may progress to cirrhosis.	3
18. Simonovsky V. The diagnosis of cirrhosis by high resolution ultrasound of the liver surface. Br J Radiol. 1999;72(853):29-34.	Observational-Dx	91 patients	To assess the clinical usefulness of high resolution ultrasound (US) analysis of the liver surface for the diagnosis of cirrhosis.	On 91 diagnostic studies, the sensitivity of US for cirrhosis was 91.1%, the specificity 93.5% and the accuracy 92.3%. Positive and negative predictive values were 93.2% and 91.5%, respectively. Provided non-diagnostic cases were considered as technically satisfactory studies and included as true-positive and false-positive cases, this would slightly increase the sensitivity but decrease specificity and accuracy to 91.8%, 84.3%, and 88.0%, respectively.	3
19. Torres WE, Whitmire LF, Gedgaudas-McClees K, Bernardino ME. Computed tomography of hepatic morphologic changes in cirrhosis of the liver. J Comput Assist Tomogr. 1986;10(1):47-50.	Observational-Dx	75 cirrhotic patients; 50 normal patients	To quantitate hepatic morphologic changes specific for cirrhosis.	The mean percentage of the total liver volume occupied by the right hepatic lobe decreased by 15.2% (p less than 0.0001) and the mean percentage of the total liver volume occupied by the medial segment of the left lobe decreased in volume by 10.9% (p less than 0.09) when compared with normals. Concomitantly, the mean percentage of the total liver volume occupied by the caudate lobe increased by 192% (p less than 0.0001) and the mean percentage of the total liver volume occupied by the lateral segment of the left lobe increased by 55.6% (p less than 0.0001). This increase in the volume of the lateral segment of the left lobe and decrease in the volume of the medial segment of the left lobe have not been described previously.	3

* See Last Page for Key

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. Lafortune M, Matricardi L, Denys A, Favret M, Dery R, Pomier-Layrargues G. Segment 4 (the quadrate lobe): a barometer of cirrhotic liver disease at US. <i>Radiology</i> . 1998;206(1):157-160.	Observational-Dx	167 patients with cirrhosis, 125 control subjects	To evaluate the dimensions of segment 4 of the liver in patients with cirrhosis by using ultrasonography (US).	In the control subject group, the mean diameter of segment 4 was 43 mm +/- 8 (standard deviation). In the patient group, the mean diameter of segment 4 was 28 mm +/- 9. The cause or severity of cirrhosis had no influence on the size of segment 4.	2
21. Ito K, Mitchell DG, Kim MJ, Awaya H, Koike S, Matsunaga N. Right posterior hepatic notch sign: a simple diagnostic MR finding of cirrhosis. <i>J Magn Reson Imaging</i> . 2003;18(5):561-566.	Observational-Dx	202 patients with pathologically proved cirrhosis. 128 without clinical evidence of chronic liver diseases.	To determine the frequency of occurrence of the right posterior hepatic notch sign at MR imaging in patients with cirrhosis, and to assess its diagnostic capability of this sign as a simple diagnostic MR finding of cirrhosis.	The right posterior hepatic notch sign was observed in 145 of the 202 patients in the cirrhosis group, while this sign was seen in only two of the 128 patients in the control group (P < 0.0001). The sensitivity, specificity, and accuracy of this sign for the MR diagnosis of cirrhosis were 72%, 98%, and 82%, respectively. When the presence of either the expanded gallbladder fossa sign or the right posterior hepatic notch sign was considered for the MR diagnosis of cirrhosis, the sensitivity and accuracy increased to 86% and 89%, respectively.	2
22. Tan KC. The right posterior hepatic notch sign. <i>Radiology</i> . 2008;248(1):317-318.	Review/Other-Dx	N/A	To describe the appearance of the posterior hepatic notch sign as seen on axial computed tomography (CT) and magnetic resonance (MR) images.	No results stated in abstract.	4
23. Ito K, Mitchell DG, Gabata T, Hussain SM. Expanded gallbladder fossa: simple MR imaging sign of cirrhosis. <i>Radiology</i> . 1999;211(3):723-726.	Observational-Dx	313 patients: 190 with pathologically proved cirrhosis, 123 without history of chronic liver diseases.	To determine the frequency on magnetic resonance (MR) images of a widened pericholecystic space, which the authors call the expanded gallbladder fossa sign, and to assess the sensitivity and specificity of this sign for cirrhosis.	The expanded gallbladder fossa sign was seen in 129 cirrhosis patients and in three control subjects (P < .001). The sensitivity, specificity, accuracy, and positive predictive value of this sign for the MR diagnosis of cirrhosis were 68%, 98%, 80%, and 98%, respectively.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
24. Yu JS, Shim JH, Chung JJ, Kim JH, Kim KW. Double contrast-enhanced MRI of viral hepatitis-induced cirrhosis: correlation of gross morphological signs with hepatic fibrosis. Br J Radiol. 2010;83(987):212-217.	Observational-Dx	111 patients	To evaluate the diagnostic ability of the expanded gallbladder fossa and right posterior hepatic notch signs for hepatic fibrosis determined by double contrast-enhanced MRI.	The expanded gallbladder fossa sign gradually increased with an increasing degree of fibrosis (Group 1, 50%; Group 2, 61%; Group 3, 78%), and there was no significant difference ($p>0.5$) between hepatitis B (67%) and C (73%). In the case of the right posterior hepatic notch sign, only 6% of Group 1 and Group 2 patients were positive; 27% of hepatitis B patients and 90% of hepatitis C patients in Group 3 exhibited the sign ($p<0.05$). Owing to its low prevalence, even in advanced cirrhosis, the right posterior hepatic notch sign is of little value in the diagnosis of cirrhosis due to chronic hepatitis B virus infection, whereas an expanded gallbladder fossa could be used as a non-specific indicator of early fibrosis before the gross appearance of advanced hepatic fibrosis.	3
25. Zhang Y, Zhang XM, Prowda JC, et al. Changes in hepatic venous morphology with cirrhosis on MRI. J Magn Reson Imaging. 2009;29(5):1085-1092.	Observational-Dx	159 patients	To identify changes in vascular morphology on magnetic resonance imaging (MRI) in patients with cirrhosis and to compare these findings to liver donors.	Hepatic veins were smaller in patients with cirrhosis (4.9, 4.5, and 5.0 mm for right, middle, and left vs. 9.9, 7.6, and 8.9 mm in donors, $P \ll 0.001$) and were negatively correlated with cirrhosis ($P < 0.001$). Right hepatic vein (RHV) <5 mm diagnosed cirrhosis with 59% sensitivity and 99% specificity; the sensitivity and specificity were 88% and 85% for RHV <7 mm. Main portal vein was minimally larger in cirrhosis, 14 versus 12 mm ($P < 0.001$) in donors. Right portal veins were smaller in cirrhotic patients, 6.5 and 6.2 mm compared to 8.4 and 7.6 mm ($P \ll 0.001$), respectively, in donors.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
26. Awaya H, Mitchell DG, Kamishima T, Holland G, Ito K, Matsumoto T. Cirrhosis: modified caudate-right lobe ratio. <i>Radiology</i> . 2002;224(3):769-774.	Observational-Dx	236 patients: 121 with pathologically proved cirrhosis and 115 without history of chronic hepatic diseases.	To determine whether a modified caudate-right lobe ratio (C/RL) with use of the right portal vein to set the lateral boundary (C/RL-r) is more accurate for diagnosing cirrhosis and evaluating its clinical severity than is the previously described C/RL with use of the main portal vein to set the lateral boundary (C/RL-m).	The area below the ROC curve was greater for C/RL-r (0.797) than for C/RL-m (0.731; P =.040). By using a C/RL-r greater than 0.90, the sensitivity, specificity, and accuracy for the MR imaging diagnosis of cirrhosis were 71.7%, 77.4%, and 74.2%, respectively. The highest accuracy of the C/RL-m was 65.7%, when the C/RL-m was greater than 0.55. Interobserver agreement was statistically confirmed for both measurements by using kappa analysis. Significant differences were found among the three Child-Pugh classes by using C/RL-r (P =.0105) but not by using C/RL-m.	3
27. Giorgio A, Amoroso P, Lettieri G, et al. Cirrhosis: value of caudate to right lobe ratio in diagnosis with US. <i>Radiology</i> . 1986;161(2):443-445	Observational-Dx	156 patients and 25 healthy subjects	To verify the value of ultrasound (US) in the diagnosis of cirrhosis.	The C/RL ratio had a sensitivity of 43%, a specificity of 100%, and an accuracy of 79% in cirrhosis. The sensitivity was very low in alcoholic cirrhosis, low in cryptogenic cirrhosis, and high in hepatitis B virus related cirrhosis.	2
28. Tan KC. Enlargement of the hilar periportal space. <i>Radiology</i> . 2008;248(2):699-700.	Review/Other-Dx	N/A	To describe the enlargement of the hilar periportal space is seen on cross-sectional images, including computed tomographic (CT) and transverse T1- and T2-weighted magnetic resonance (MR) images.	On MR images, the mean hilar periportal fat thickness in patients without hepatic cirrhosis was found to be 5.3 mm ± 3.1 (standard deviation) (range, 0–11 mm) (2). In patients with hepatic cirrhosis, this increases to 15.5 mm ± 6.2.	4
29. Ito K, Mitchell DG, Gabata T. Enlargement of hilar periportal space: a sign of early cirrhosis at MR imaging. <i>J Magn Reson Imaging</i> . 2000;11(2):136-140.	Observational-Dx	41 pathologically proved cirrhotic patients and 47 patients without history of chronic liver diseases	To determine whether the finding of an enlarged hilar periportal space is a sign for early cirrhosis at magnetic resonance (MR) imaging.	Enlargement of the periportal space was seen in 98% of patients in the early cirrhosis group, while this finding was seen in 11% of patients in the control group (P < 0.0001). The mean value of the hilar periportal fat thickness was significantly greater (P < 0.0001) in the early cirrhosis group (15.5 +/- 6.2 mm) than in the control group (5.3 +/- 3.1 mm). The sensitivity, specificity, accuracy, and positive predictive value of this finding for the MR diagnosis of cirrhosis with a cutoff value of 10 mm were 93%, 92%, 92%, and 91%, respectively.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
30. Colli A, Colucci A, Paggi S, et al. Accuracy of a predictive model for severe hepatic fibrosis or cirrhosis in chronic hepatitis C. World J Gastroenterol. 2005;11(46):7318-7322.	Observational-Dx	176 patients	To assess the accuracy of a model in diagnosing severe fibrosis/cirrhosis in chronic hepatitis C virus (HCV) infection.	Severe fibrosis/cirrhosis was found in 67 patients (38%). The model discriminated patients in three comparable groups: 34% with a very high (>90%) or low (<10%) probability of severe fibrosis, 33% with a probability ranging from 75% to 90%, and 33% with an uncertain diagnosis (i.e., a probability ranging from 10% to 74%). The observed frequency of severe fibrosis/cirrhosis was within the predefined ranges.	2
31. Bonekamp S, Kamel I, Solga S, Clark J. Can imaging modalities diagnose and stage hepatic fibrosis and cirrhosis accurately? J Hepatol. 2009;50(1):17-35.	Review/Other-Dx	N/A	To assess performance and promise of radiologic modalities and techniques as alternative, noninvasive assessment of hepatic fibrosis.	A systematic review revealed accurate staging of fibrosis or diagnosis of mild fibrosis was often not achievable. Ultrasonography is the most common modality used in the diagnosis and staging of hepatic fibrosis. Elastographic measurements, either ultrasonography-based or magnetic resonance-based, and magnetic resonance diffusion weighted imaging, show the most promise for accurate staging of hepatic fibrosis. Most currently available imaging techniques can detect cirrhosis or significant fibrosis reasonably accurately. However, to date only magnetic resonance elastography has been able to stage fibrosis or diagnose mild disease.	4
32. Tchelepi H, Ralls PW, Radin R, Grant E. Sonography of diffuse liver disease. J Ultrasound Med. 2002;21(9):1023-1032; quiz 1033-1024.	Review/Other-Dx	N/A	To discuss the uses and limitations of sonography in evaluating parenchymal liver disease.	Sonography is of limited usefulness in acute hepatitis. Increased parenchymal echogenicity is a reliable criterion for diagnosing fatty liver. Cirrhosis can be diagnosed in the correct clinical setting when the following are present: a nodular liver surface, decreased right lobe-caudate lobe ratio, and indirect evidence of portal hypertension (collateral vessels and splenomegaly).	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Haktanir A, Cihan BS, Celenk C, Cihan S. Value of Doppler sonography in assessing the progression of chronic viral hepatitis and in the diagnosis and grading of cirrhosis. <i>J Ultrasound Med.</i> 2005;24(3):311-321.	Observational-Dx	36 patients with chronic viral hepatitis, 63 patients with cirrhosis, and 30 control subjects with no evidence of liver disease.	To evaluate the value of Doppler sonography in assessing the progression of chronic viral hepatitis and in the diagnosis and grading of cirrhosis.	The most useful indices were portal vein velocity, the modified hepatic index, and nontriphasic flow in the hepatic vein, which were helpful in distinguishing patients from control subjects. Hepatic vascular and modified hepatic indices were useful for differential diagnosis of cirrhosis and chronic viral hepatitis. However, all measurements were limited in their ability to determine the severity of chronic hepatitis.	2
34. Kawanaka H, Kinjo N, Anegawa G, et al. Abnormality of the hepatic vein waveforms in cirrhotic patients with portal hypertension and its prognostic implications. <i>J Gastroenterol Hepatol.</i> 2008;23(7 Pt 2):e129-136.	Observational-Dx	103 patients	To investigate the prognostic significance of changes in the Doppler hepatic vein (HV) waveforms in cirrhotic patients with portal hypertension and the mechanisms of these changes.	Type I was observed in 34, type II in 40, type III in 23, and type IV in six patients. The 5-year survival rates were 90%, 89%, 41%, and 0% in type I, II, III, and IV, respectively. Five variables including the Child-Pugh score, albumin, bilirubin, ascites, and HV waveform significantly correlated with the survival in a univariate analysis. A multivariate analysis only identified the HV waveform (type III and IV) to be an independent prognostic value. Even in Child-Pugh class B patients, the 5-year survival rate for type III or IV was as poor as 26% in comparison to 92% for type I or II. In contrast, in Child-Pugh class C patients, the 5-year survival rate for type I or II was as good as 63% in comparison to 25% for type III or IV. Furthermore, the changes in HV waveforms correlated with the extent of hepatic fibrosis, the increase in portal perfusion per liver volume, or the decrease in portal vascular resistance.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Oguzkurt L, Yildirim T, Torun D, Tercan F, Kizilkilic O, Niron EA. Hepatic vein Doppler waveform in patients with diffuse fatty infiltration of the liver. <i>Eur J Radiol.</i> 2005;54(2):253-257.	Observational-Dx	40 patients with diffuse FIL and 50 normal healthy adults	To determine the incidence of abnormal hepatic vein Doppler waveform in patients with diffuse fatty infiltration of the liver (FIL).	Seventeen of the 40 patients (43%) with FIL had an abnormal HV Doppler waveform, whereas only one of the 50 (2%) healthy subjects had an abnormal waveform. The difference in the distribution of normal Doppler waveform pattern between the patients and the control group was significant ($P < 0.001$). No differences were found in the behaviour of the hepatic vein Doppler waveform in relation to the different etiologic factors for FIL ($P > 0.05$). There was not any correlation between the degree of fat infiltration and the hepatic vein waveform pattern ($P = 0.60$).	3
36. Bernatik T, Strobel D, Hahn EG, Becker D. Doppler measurements: a surrogate marker of liver fibrosis? <i>Eur J Gastroenterol Hepatol.</i> 2002;14(4):383-387.	Observational-Dx	43 patients	To assess the correlation between Doppler measurements and histologically proven liver fibrosis.	Sixty-seven per cent of the patients in our study group had no or only mild fibrosis (Ludwig score stage I or II). Thirty-three per cent showed progressive fibrosis or cirrhosis (Ludwig score stage III or IV). There was a large overlap in the Doppler measurements and findings between the various disease stages. No significant changes of Doppler parameters were detected, even between patients with no or mild fibrosis and patients with severe fibrosis (Ludwig score stage III or IV).	3
37. Talwalkar JA, Kurtz DM, Schoenleber SJ, West CP, Montori VM. Ultrasound-based transient elastography for the detection of hepatic fibrosis: systematic review and meta-analysis. <i>Clin Gastroenterol Hepatol.</i> 2007;5(10):1214-1220.	Meta-analysis	9 studies	To perform a systematic review and meta-analysis of diagnostic accuracy studies comparing ultrasound-based transient elastography with liver biopsy for hepatic fibrosis.	Nine studies in full publication were identified. For patients with stage IV fibrosis (cirrhosis), the pooled estimates for sensitivity were 87% (95% confidence interval [CI], 84%-90%), specificity 91% (95% CI, 89%-92%), positive likelihood ratio 11.7 (95% CI, 7.9-17.1), and negative likelihood ratio 0.14 (95% CI, 0.10-0.20). Among 7 investigations reporting patients with stages II-IV fibrosis, the pooled estimates for sensitivity were 70% (95% CI, 67%-73%), specificity 84% (95% CI, 80%-88%), positive likelihood ratio 4.2 (95% CI, 2.4-7.2), and negative likelihood ratio 0.31 (95% CI, 0.23-0.43). Diagnostic threshold (or cut-off value) bias was identified as an important cause of heterogeneity for pooled results in both patient groups.	M

* See Last Page for Key

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Degos F, Perez P, Roche B, et al. Diagnostic accuracy of FibroScan and comparison to liver fibrosis biomarkers in chronic viral hepatitis: a multicenter prospective study (the FIBROSTIC study). J Hepatol. 2010;53(6):1013-1021.	Experimental-Dx	1307 patients	To assess and compare the accuracy of FibroScan(R) and that of the main biomarkers used for predicting cirrhosis and significant fibrosis (METAVIR \geq F2) in patients with chronic viral hepatitis.	The analysis was first conducted on the total population (1839 patients), and after excluding 532 protocol deviations, on 1307 patients (non-compliant FibroScan(R) examinations). The overall accuracy of FibroScan(R) was high (AUROC 0.89 and 0.90, respectively) and significantly higher than that of biomarkers in predicting cirrhosis (AUROC 0.77-0.86). All non-invasive methods had a moderate accuracy in predicting significant fibrosis (AUROC 0.72-0.78). Based on multilevel likelihood ratios, non-invasive tests provided a relevant gain in the likelihood of diagnosis in 0-60% of patients (cirrhosis) and 9-30% of patients (significant fibrosis).	1
39. Myers RP, Pomier-Layrargues G, Kirsch R, et al. Discordance in fibrosis staging between liver biopsy and transient elastography using the FibroScan XL probe. J Hepatol. 2012;56(3):564-570.	Observational-Dx	210 patients	To examine the prevalence, risk factors, and causes of discordance between fibrosis estimated by the FibroScan XL probe and biopsy.	Fibrosis estimated by the FibroScan XL probe was greater than biopsy in 75% (18/24) of discordant cases. Although biopsy quality was not associated with discordance, discordant cases were less likely to have \geq 10 valid shots (75% vs. 97%; $p=0.001$), a success rate \geq 60% (67% vs. 95%; $p < 0.0005$), and an interquartile range over median liver stiffness (IQR/M) $< 21\%$ (37% vs. 57%; $p=0.07$) than non-discordant cases. However, only increased BMI (odds ratio [OR] 1.09 per kg/m^2 ; 95% confidence interval [CI] 1.01-1.18; $p=0.04$) was independently associated with discordance; liver stiffness was of borderline significance (OR 1.73 per $\log(10)$ -transformed value; 95% CI 0.95-3.18; $p=0.08$). Discordance was 4- to 5-fold more frequent among patients with severe obesity (BMI $\geq 40 \text{ kg}/\text{m}^2$: 32% vs. 8%) and liver stiffness above the median of 7.0 kPa (20% vs. 4%; both $p < 0.0005$).	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
40. Yoneda M, Suzuki K, Kato S, et al. Nonalcoholic fatty liver disease: US-based acoustic radiation force impulse elastography. <i>Radiology</i> . 2010;256(2):640-647.	Observational-Dx	54 patients with a liver biopsy-confirmed diagnosis of nonalcoholic fatty liver disease (NAFLD)	To investigate the clinical usefulness of ultrasonography-based acoustic radiation force impulse (ARFI) elastography (ie, ARFI sonoelastography) in patients with a diagnosis of nonalcoholic fatty liver disease (NAFLD) and compare ARFI sonoelastography results with transient sonoelastography and serum fibrosis marker test results.	Median velocities in the patients with NAFLD were 1.040 m/sec for those with stage 0 fibrosis, 1.120 m/sec for those with stage 1, 1.130 m/sec for those with stage 2, 1.780 m/sec for those with stage 3, and 2.180 m/sec for those with stage 4. The A(z) for the diagnosis of hepatic fibrosis stages 3 or higher was 0.973 (optimal cutoff value, 1.77 m/sec; sensitivity, 100%; specificity, 91%), while that for the diagnosis of stage 4 fibrosis was 0.976 (optimal cutoff value, 1.90 m/sec; sensitivity, 100%; specificity, 96%). Significant correlations between median velocity measured by using ARFI sonoelastography and the following parameters were observed: liver stiffness measured with transient sonoelastography (r = 0.75, P < .0001), serum level of hyaluronic acid (r = 0.459, P = .0009), and serum level of type IV collagen 7 S domain (r = 0.445, P = .0015).	1
41. Palmeri ML, Wang MH, Rouze NC, et al. Noninvasive evaluation of hepatic fibrosis using acoustic radiation force-based shear stiffness in patients with nonalcoholic fatty liver disease. <i>J Hepatol</i> . 2011;55(3):666-672.	Observational-Dx	172 patients diagnosed with NAFLD	To evaluate ARFI shear wave imaging as a potential non-invasive method to assess the hepatic fibrosis stage in patients with biopsy-proven NAFLD.	Reconstructed shear stiffnesses were not associated with ballooned hepatocytes (p=0.11), inflammation (p=0.69), nor imaging location (p=0.11). Using a predictive shear stiffness threshold of 4.24kPa, shear stiffness distinguished low (fibrosis stage 0-2) from high (fibrosis stage 3-4) fibrosis stages with a sensitivity of 90% and a specificity of 90% (AUC of 0.90). Shear stiffness had a mild correlation with APRI (R(2)=0.22). BMI>40kg/m(2) was not a limiting factor for ARFI imaging, and no correlation was noted between BMI and shear stiffness (R(2)=0.05).	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Ochi H, Hirooka M, Koizumi Y, et al. Real-time tissue elastography for evaluation of hepatic fibrosis and portal hypertension in nonalcoholic fatty liver diseases. <i>Hepatology</i> . 2012;56(4):1271-1278.	Observational-Dx	181 patients	To prospectively measure liver stiffness with real-time tissue elastography in patients with nonalcoholic fatty liver diseases (NAFLD) and to compare the result with the clinical assessment of fibrosis using histological stage.	Real-time tissue elastography cut-off values by stage in the training set were 2.47 for F1, 2.67 for F2, 3.02 for F3, and 3.36 for F4. Using these cut-off values, the diagnostic accuracy of hepatic fibrosis in the validation set was 82.6%-96.0% in all stages. Only portal fibrosis correlated with the hepatic elastic ratio by multivariate analysis. The area under the receiver operating characteristic curve of elastic ratio better correlated than serum fibrosis markers in both early and advanced fibrosis stages. Patients with PH, defined by splenic elasticity, had early fibrosis. Patients with severe PH were found only in the group with cirrhosis.	2
43. Bota S, Herkner H, Sporea I, et al. Meta-analysis: ARFI elastography versus transient elastography for the evaluation of liver fibrosis. <i>Liver Int</i> . 2013;33(8):1138-1147.	Meta-analysis	1163 patients with chronic hepatopathies	To compare the diagnostic performance of acoustic radiation force impulse (ARFI) elastography and transient elastography (TE) in the assessment of liver fibrosis using liver biopsy (LB) as 'gold-standard'.	Thirteen studies (11 full-length articles and 2 abstracts) including 1163 patients with chronic hepatopathies were included in the analysis. Inability to obtain reliable measurements was more than thrice as high for TE as that of ARFI (6.6% vs. 2.1%, $P < 0.001$). For detection of significant fibrosis, ($F \geq 2$) the summary sensitivity (Se) was 0.74 (95% CI: 0.66-0.80) and specificity (Sp) was 0.83 (95% CI: 0.75-0.89) for ARFI, while for TE the Se was 0.78 (95% CI: 0.72-0.83) and Sp was 0.84 (95% CI: 0.75-0.90). For the diagnosis of cirrhosis, the summary Se was 0.87 (95% CI: 0.79-0.92) and Sp was 0.87 (95% CI: 0.81-0.91) for ARFI elastography, and, respectively, 0.89 (95% CI: 0.80-0.94) and 0.87 (95% CI: 0.82-0.91) for TE. The diagnostic odds ratio of ARFI and TE did not differ significantly in the detection of significant fibrosis [mean difference in rDOR = 0.27 (95% CI: 0.69-0.14)] and cirrhosis [mean difference in rDOR = 0.12 (95% CI: 0.29-0.52)].	M

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Arena U, Vizzutti F, Corti G, et al. Acute viral hepatitis increases liver stiffness values measured by transient elastography. <i>Hepatology</i> . 2008;47(2):380-384.	Observational-Dx	18 patients	To definitively assess the influence of necro-inflammation on liver stiffness measurement (LSM).	In all patients, the degree of liver stiffness at the time of the peak increase in aminotransferases exceeded the cutoff values proposed for the prediction of significant fibrosis or cirrhosis. A progressive significant reduction in liver stiffness values was observed (P<0.0001) in the follow-up period in parallel with the reduction of aminotransferase levels (P < 0.0001). Moreover, a statistically significant, positive correlation between aminotransferases and liver stiffness measurement (LSM) at the onset of acute viral hepatitis was found (r = 0.53, P = 0.02 and r = 0.51, P = 0.03 for alanine aminotransferase and aspartate aminotransferase, respectively). (r 0.53, P 0.02 and	2
45. Millonig G, Reimann FM, Friedrich S, et al. Extrahepatic cholestasis increases liver stiffness (FibroScan) irrespective of fibrosis. <i>Hepatology</i> . 2008;48(5):1718-1723.	Observational-Dx	15 patients presenting with extrahepatic cholestasis	To determine if the measurement of liver stiffness by FS is altered in patients with extrahepatic cholestasis.	Initially elevated liver stiffness decreased in 13 of 15 patients after intervention, in 10 of them markedly. In three patients, liver stiffness was elevated to a degree that suggested advanced liver cirrhosis (mean, 15.2 kPa). Successful drainage led to a drop of bilirubin by 2.8 to 9.8 mg/dL whereas liver stiffness almost normalized (mean, 7.1 kPa). In all patients with successful biliary drainage, the decrease of liver stiffness highly correlated with decreasing bilirubin (Spearman's p = 0.67, P < 0.05) with a mean decrease of liver stiffness of 1.2 +/- 0.56 kPa per 1 g/dL bilirubin. Two patients, in whom liver stiffness did not decrease despite successful biliary drainage, had advanced liver cirrhosis and multiple liver metastases, respectively.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Millonig G, Friedrich S, Adolf S, et al. Liver stiffness is directly influenced by central venous pressure. <i>J Hepatol.</i> 2010;52(2):206-210.	Experimental-Dx	10 patients and 8 pigs	To determine whether hemodynamic changes affect liver stiffness irrespective of fibrosis.	Initial LS was elevated in all patients, in 8 of them to a degree that suggested liver cirrhosis (median 40.7kPa). Upon recompensation with a median weight loss of 3.0kg, LS decreased in all 10 patients down to a median LS of 17.8kPa. Inflammation could not account for increased LS since initial liver enzyme counts were only slightly elevated and did not change significantly.	3
47. Mederacke I, Wurstthorn K, Kirschner J, et al. Food intake increases liver stiffness in patients with chronic or resolved hepatitis C virus infection. <i>Liver Int.</i> 2009;29(10):1500-1506.	Observational-Dx	56 patients and 19 controls	To assess whether food intake, that increases liver blood flow, influences liver stiffness.	Liver stiffness significantly increased immediately after food intake for up to 60 min (P=0.01) before normalizing after 180 min. An intraindividual analysis showed a significant increase in 22 out of 43 patients with an initial liver stiffness ≤ 10 kPa. An increase of at least 1 kPa after food intake was found in 24 out of 43 (56%) patients with initial stiffness ≤ 10 kPa. Notably, nine out of 23 (39%) patients with normal initial liver stiffness (< 6 kPa) had a value of > 6 kPa after food intake, potentially leading to unnecessary treatment or diagnostic procedures.	3
48. Popescu A, Bota S, Sporea I, et al. The influence of food intake on liver stiffness values assessed by acoustic radiation force impulse elastography-preliminary results. <i>Ultrasound Med Biol.</i> 2013;39(4):579-584.	Observational-Dx	73 healthy subjects with no history of liver disease.	To assess the influence of food intake on acoustic radiation force impulse elastography (ARFI) measurements.	In the study group, the mean liver stiffness (LS) values by ARFI increased significantly 1 h after food intake (1.51 +/- 0.40 m/s vs. 1.27 +/- 0.23, p = 0.003), but 3 h after the meal the differences were no longer significant (1.46 +/- 0.51 vs. 1.27 +/- 0.23, p = 0.06). In the control group, the mean LS values were similar in all 3 measurements.	3
49. Bonekamp D, Bonekamp S, Geiger B, Kamel IR. An elevated arterial enhancement fraction is associated with clinical and imaging indices of liver fibrosis and cirrhosis. <i>J Comput Assist Tomogr.</i> 2012;36(6):681-689.	Observational-Dx	65 patients	To determine whether arterial enhancement fraction (AEF) is associated with the degree of liver fibrosis and cirrhosis in patients with chronic liver disease	Mean AEF was higher in patients with liver disease compared with those without liver disease. Mean AEF differed significantly between patients with normal liver or mild fibrosis (category 1), moderate to severe fibrosis (category 2), and cirrhosis (category 3). Receiver operating characteristic curve analysis determined an area under the curve of 0.79/0.78, with an optimal cutoff for mean AEF of 9.2/16.8, for differentiating between category 2 or higher/category 3 disease.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Lv P, Lin X, Gao J, Chen K. Spectral CT: preliminary studies in the liver cirrhosis. Korean J Radiol. 2012;13(4):434-442.	Observational-Dx	38 patients with liver cirrhosis and 43 patients with healthy livers. Triple-phase CT (one phase with and two without contrast) was performed.	To investigate the value of spectral CT imaging in the diagnosis and classification of liver cirrhosis during the arterial phase (AP) and portal venous phase (PVP).	The mean normalized iodine concentration (NIC) (0.5 +/- 0.12) during PVP in the control group was significantly higher than that in the study group (0.4 +/- 0.10 on average, 0.4 +/- 0.08 for Class A, 0.4 +/- 0.15 for Class B, and 0.4 +/- 0.06 for Class C) (All p < 0.05). Within the cirrhotic liver group, the mean NIC for Class C during the AP (0.1 +/- 0.05) was significantly higher than NICs for Classes A (0.1 +/- 0.06) and B (0.1 +/- 0.03) (Both p < 0.05). The IC(ratio) in the study group (0.4 +/- 0.15), especially for Class C (0.5 +/- 0.14), was higher than that in the control group (0.3 +/- 0.15) (p < 0.05). The combination of NIC and IC(ratio) showed high sensitivity and specificity for differentiating healthy liver from cirrhotic liver, especially in Class C cirrhotic liver.	3
51. Ronot M, Asselah T, Paradis V, et al. Liver fibrosis in chronic hepatitis C virus infection: differentiating minimal from intermediate fibrosis with perfusion CT. Radiology. 2010;256(1):135-142.	Observational-Dx	52 patients	To prospectively assess the utility of perfusion computed tomography (CT) for differentiating minimal from intermediate fibrosis in treatment-naïve patients with chronic hepatitis C virus (HCV) infection.	In patients with intermediate fibrosis (F2 and F3) compared with those with minimal fibrosis (F1), the portal venous perfusion (87 mL min(-1) 100 mL(-1) +/- 27 [standard deviation] vs 138 mL min(-1) 100 mL(-1) +/- 112, P = .042) and total liver perfusion (107 mL min(-1) 100 mL(-1) +/- 31 vs 169 mL min(-1) 100 mL(-1) +/- 137, P = .02) were significantly decreased, and the mean transit time was significantly increased (16 seconds +/- 4 vs 13 seconds +/- 5, P = .025). At multivariate analysis, only the mean transit time was an independent factor (odds ratio, 1.18; 95% confidence interval: 1.02, 1.37; P = .030). Receiver operating characteristic curve analysis showed that a mean transit time threshold of 13.4 seconds allowed discrimination between minimal and intermediate fibrosis with a sensitivity of 71% and a specificity of 65%.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Zhao LQ, He W, Yan B, Wang HY, Wang J. The evaluation of haemodynamics in cirrhotic patients with spectral CT. Br J Radiol. 2013;86(1028):20130228.	Observational-Dx	21 patients; All subjects underwent three-phase spectral CT scans.	To evaluate haemodynamics in cirrhotic patients with portal hypertension using spectral CT imaging.	The AIF was 0.25+/-0.05 in the control group, and 0.29+/-0.10, 0.37+/-0.12 and 0.43+/-0.14 in the study group with Child-Pugh Grades A, B and C, respectively. The difference in AIF between the control and study groups was statistically significant. The differences were statistically significant between the subgroups with multiple comparisons except between the control group and the Child-Pugh A group (p=0.685).	3
53. Martin DR, Lauenstein T, Kalb B, et al. Liver MRI and histological correlates in chronic liver disease on multiphase gadolinium-enhanced 3D gradient echo imaging. J Magn Reson Imaging. 2012;36(2):422-429.	Observational-Dx	75 patients	To evaluate intrinsic hepatic enhancement patterns on multiphase, gadolinium-enhanced, fat-suppressed, 3D T1-weighted, gradient echo magnetic resonance imaging (MRI) as a quantitative correlate for severity of pathological changes in chronic liver disease (CLD).	MRI histology correlation was high for delayed-phase MRI versus fibrosis stage (95% confidence interval [CI] 0.941 < r < 0.976, P = 5 x 10(-7)), but lower for all other comparisons (delayed-phase vs. inflammation and arterial-phase vs. inflammation or fibrosis all showed a CI no greater than 0.64). Paired testing between delayed-phase MRI score and histology fibrosis staging incremental levels was significant (from P < 10(-2) to P < 10(-5)).	2
54. Singh S, Venkatesh SK, Wang Z, et al. Diagnostic performance of magnetic resonance elastography in staging liver fibrosis: a systematic review and meta-analysis of individual participant data. Clin Gastroenterol Hepatol. 2015;13(3):440-451 e446.	Meta-analysis	12 Studies including 697 patients	To assess the diagnostic accuracy of MRE for staging liver fibrosis in patients with chronic liver diseases (CLD).	We analyzed data from 12 retrospective studies, comprising 697 patients (mean age, 55 +/- 13 y; 59.4% male; mean BMI, 26.9 +/- 6.7 kg/m(2); 92.1% with <1 year interval between MRE and biopsy; and 47.1% with hepatitis C). Overall, 19.5%, 19.4%, 15.5%, 15.9%, and 29.7% patients had stage 0, 1, 2, 3, and 4 fibrosis, respectively. The mean area under the receiver-operating curve values (and 95% confidence intervals) for the diagnosis of any (>=stage 1), significant (>=stage 2), advanced fibrosis (>=stage 3), and cirrhosis, were as follows: 0.84 (0.76-0.92), 0.88 (0.84-0.91), 0.93 (0.90-0.95), and 0.92 (0.90-0.94), respectively. A similar diagnostic performance was observed in stratified analysis based on sex, obesity, and etiology of CLD. The overall rate of failure of MRE was 4.3%	M

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Castera L, Foucher J, Bernard PH, et al. Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 examinations. <i>Hepatology</i> . 2010;51(3):828-835.	Observational-Dx	13,369 examinations	To investigate the frequency and determinants of LSM failure and unreliable results over a 5-year period.	LSM failure occurred in 3.1% of all examinations (4% at first examination [n = 7261]) and was independently associated at first examination with body mass index (BMI) greater than 30 kg/m ² (odds ratio [OR], 7.5; 95% confidence interval [CI], 5.6-10.2; P = 0.0001), operator experience fewer than 500 examinations (OR 2.5 [1.6-4.0]; P = 0.0001); age greater than 52 years (OR 2.3 [1.6-3.2]; P = 0.0001), and type 2 diabetes (OR 1.6 [1.1-2.2]; P = 0.009). Unreliable results were obtained in a further 15.8% of cases (17% at first examination) and were independently associated at first examination with BMI greater than 30 kg/m ² (OR 3.3 [2.8-4.0]; P = 0.0001), operator experience fewer than 500 examinations (OR 3.1 [2.4-3.9]; P = 0.0001), age greater than 52 years (OR 1.8 [1.6-2.1]; P = 0.0001), female sex (OR 1.4 [1.2-1.6]; P = 0.0001), hypertension (OR 1.3 [1.1-1.5]; P = 0.003), and type 2 diabetes (OR 1.2 [1.0-1.5]; P = 0.05). When metabolic syndrome and waist circumference were taken into account in a subgroup of 2835 patients, waist circumference was the most important determinant of LSM failure and unreliable results.	3
56. Bota S, Sporea I, Sirlu R, et al. Factors associated with the impossibility to obtain reliable liver stiffness measurements by means of Acoustic Radiation Force Impulse (ARFI) elastography--analysis of a cohort of 1,031 subjects. <i>Eur J Radiol</i> . 2014;83(2):268-272.	Meta-analysis	13 studies including 1,163 patients	To assess the feasibility of ARFI elastography in a large cohort of subjects and to identify factors associated with impossibility to obtain reliable liver stiffness (LS) measurements by means of this technique.	Failure of LS measurements by means of ARFI was observed in 4 subjects (0.3%), unreliable measurements in 66 subjects (6.4%), so reliable measurements were obtained in 961 subjects (93.3%). In univariate analysis, the following risk factors were associated with failed and unreliable measurements: age over 58 years (OR=0.49; 95% CI 0.30-0.80, p=0.005), male gender (OR=0.58; 95% CI 0.34-0.94, p=0.04), BMI>27.7 kg/m ² (OR=0.23, 95% CI 0.13-0.41, p<0.0001). In multivariate analysis all the factors mentioned above were independently associated with the risk of failed and unreliable measurements.	M

* See Last Page for Key

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Huwart L, Sempoux C, Vicaut E, et al. Magnetic resonance elastography for the noninvasive staging of liver fibrosis. <i>Gastroenterology</i> . 2008;135(1):32-40.	Observational-Dx	141 patients	To prospectively compare the success rate and diagnostic accuracy of magnetic resonance elastography, ultrasound elastography, and aspartate aminotransferase to platelets ratio index (APRI) measurements for the noninvasive staging of fibrosis in patients with chronic liver disease.	A total of 141 patients were assessed. The technical success rate of magnetic resonance elastography was higher than that of ultrasound elastography (133/141 [94%] vs 118/141 [84%]; P = .016). Magnetic and ultrasound elastography, APRI measurements, and histopathologic analysis of liver biopsy specimens were technically successful in 96 patients. The areas under the receiver operating characteristic curves of magnetic resonance elasticity (0.994 for F ≥ 2; 0.985 for F ≥ 3; 0.998 for F = 4) were larger (P < .05) than those of ultrasound elasticity, APRI, and the combination of ultrasound elasticity and APRI (0.837, 0.709, and 0.849 for F ≥ 2; 0.906, 0.816, and 0.936 for F ≥ 3; 0.930, 0.820, and 0.944 for F = 4, respectively).	2
58. Wang QB, Zhu H, Liu HL, Zhang B. Performance of magnetic resonance elastography and diffusion-weighted imaging for the staging of hepatic fibrosis: A meta-analysis. <i>Hepatology</i> . 2012;56(1):239-247.	Meta-analysis	14 studies	To assess and compare the accuracies of magnetic resonance elastography (MRE) and diffusion-weighted imaging (DWI) for the staging of hepatic fibrosis.	With MRE, the sensitivity, specificity, DOR, PLR, NLR, and area under sROC curve (with 95% CIs) for staging F0 approximately F1 versus F2 approximately F4 and F0 approximately F2 versus F3 approximately F4 were 0.94 (0.81-0.98), 0.95 (0.87-0.98), 20 (7-57), 0.06 (0.02-0.22), 317 (55-1,796), 0.98 (0.97-0.99) and 0.92 (0.85-0.96), 0.96 (0.91-0.98), 21 (10-45), 0.08 (0.04-0.16), 251 (103-609), and 0.98 (0.96-0.99), respectively; and with DWI, these values were 0.77 (0.71-0.82), 0.78 (0.69-0.85), 3 (2-5), 0.30 (0.22-0.40), 12 (6-21), 0.83 (0.79-0.86) and 0.72 (0.60-0.81), 0.84 (0.77-0.89), 5 (3-7), 0.34 (0.23-0.50), 13 (6-29), and 0.86 (0.83-0.89), respectively. A z test demonstrated that MRE had a significantly higher accuracy than DWI in those indicators (P < 0.05).	M

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Taouli B, Tolia AJ, Losada M, et al. Diffusion-weighted MRI for quantification of liver fibrosis: preliminary experience. AJR Am J Roentgenol. 2007;189(4):799-806.	Observational-Dx	23 patients with chronic hepatitis and 7 healthy volunteers.	To evaluate our preliminary experience using diffusion-weighted MRI for quantification of liver fibrosis.	Using a b value of 500 s/mm ² and all combined b values, we found significantly lower hepatic ADCs in stage 2 or greater versus stage 1 or less fibrosis and stage 3 or greater versus stage 2 or less fibrosis. The mean ADCs (x 10 ⁻³ mm ² /s) with all b values were 1.47 +/- 0.11 (SD) versus 1.65 +/- 0.10 for stage 2 or greater versus stage 1 or less fibrosis (p < 0.001) and 1.44 +/- 0.07 versus 1.66 +/- 0.10 for stage 3 or greater versus stage 2 or less fibrosis (p < 0.001). Hepatic ADC was a significant predictor of stage 2 or greater and stage 3 or greater fibrosis, with areas under the curve of 0.896 and 0.896, sensitivity of 83.3% and 88.9%, and specificity of 83.3% and 80.0% (ADC with all b values, 1.54-1.53 x 10 ⁻³ mm ² /s or less).	3
60. Girometti R, Furlan A, Bazzocchi M, et al. Diffusion-weighted MRI in evaluating liver fibrosis: a feasibility study in cirrhotic patients. Radiol Med. 2007;112(3):394-408.	Observational-Dx	28 cirrhotic patients and 29 healthy controls.	To establish whether the measurement of apparent diffusion coefficients (ADCs) is clinically accurate in diagnosing liver fibrosis in a selected series of cirrhotic patients.	Mean ADC was significantly lower in cirrhotic livers than in controls (1.11 +/- 0.16 vs. 1.54 +/- 0.12. 10 ⁻³ mm ² /s) (p < 0.0001). Receiver operating characteristic (ROC) analysis showed an area under the curve (AUC) of 0.96 [confidence interval (CI) 95%:(0.87; 0.94)], demonstrating higher sensitivity and specificity (92.9% and 100%, respectively) for an ADC cutoff of 1.31.10 ⁻³ mm ² /s. Positive predictive value (PPV), negative predictive value (NPV) and overall accuracy were 100%, 99.9% and 96.4%, respectively	2
61. Watanabe H, Kanematsu M, Goshima S, et al. Staging hepatic fibrosis: comparison of gadoxetate disodium-enhanced and diffusion-weighted MR imaging--preliminary observations. Radiology. 2011;259(1):142-150.	Observational-Dx	114 patients Note: Contrast enhanced magnetic resonance (MR)	To evaluate the utility of hepatocyte-phase gadoxetate disodium-enhanced magnetic resonance (MR) imaging in staging hepatic fibrosis and to compare it with diffusion-weighted imaging.	Among the MR, hematologic, and clinical parameters, contrast enhancement index was most strongly correlated with fibrosis stage (r = -0.79, P < .001). Multiple regression analysis showed that the contrast enhancement index, ADC, and prothrombin time were significantly correlated (r(2) = 0.66, P < .05) with fibrosis stage and that the contrast enhancement index and serum total bilirubin level were weakly correlated (r(2) = 0.24, P < .05) with the necroinflammatory activity grade.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
62. Choi YR, Lee JM, Yoon JH, Han JK, Choi BI. Comparison of magnetic resonance elastography and gadoxetate disodium-enhanced magnetic resonance imaging for the evaluation of hepatic fibrosis. <i>Invest Radiol.</i> 2013;48(8):607-613.	Observational-Dx	168 patients	To compare the diagnostic performance of magnetic resonance elastography (MRE) and gadoxetate disodium-enhanced magnetic resonance imaging (MRI) in the staging of hepatic fibrosis (HF) in patients with liver diseases. Note: Contrast was administered.	The liver stiffness values measured on MRE ($r = 0.802$; $P < 0.0001$) were more strongly correlated with the HF stage than with the contrast enhanced index or CEI ($r = -0.378$; $P < 0.0001$). The areas under the receiver operating characteristic curve values of the liver stiffness values were significantly larger than those of CEI were for discriminating all stages of HF ($P < 0.001$ for $\geq F1$, $\geq F2$, $\geq F3$, and $\geq F4$). Magnetic resonance elastography showed higher sensitivity and specificity for predicting HF $\geq F1$ (91% and 87%), $\geq F2$ (87% and 91%), $\geq F3$ (80% and 89%), and F4 (81% and 85%) compared with CEI (46% and 85%, 46% and 82%, 63% and 68%, and 76% and 65%, respectively).	2
63. Hagiwara M, Rusinek H, Lee VS, et al. Advanced liver fibrosis: diagnosis with 3D whole-liver perfusion MR imaging--initial experience. <i>Radiology.</i> 2008;246(3):926-934.	Observational-Dx	20 patients with chronic liver disease and 7 control subjects Note: Contrast enhanced MR imaging	To prospectively evaluate sensitivity and specificity of various estimated perfusion parameters at three-dimensional (3D) perfusion magnetic resonance (MR) imaging of the liver in the diagnosis of advanced liver fibrosis (stage ≥ 3), with histologic analysis, liver function tests, or MR imaging as the reference standard.	There were significant differences for all perfusion MR imaging-estimated parameters except F(p) and F(t). There was an increase in F(a), ART, DV, and MTT and a decrease in PV in patients with advanced fibrosis compared with those without advanced fibrosis. DV had the best performance, with an area under the receiver operating characteristic curve of 0.824, a sensitivity of 76.9% (95% confidence interval: 46.2%, 94.7%), and a specificity of 78.5% (95% confidence interval: 49.2%, 95.1%) in the prediction of advanced fibrosis.	2
64. Chen BB, Hsu CY, Yu CW, et al. Dynamic contrast-enhanced magnetic resonance imaging with Gd-EOB-DTPA for the evaluation of liver fibrosis in chronic hepatitis patients. <i>Eur Radiol.</i> 2012;22(1):171-180.	Observational-Dx	79 patients (21 in the healthy group and 58 in the hepatitis group)	To develop a non-invasive MRI method for evaluation of liver fibrosis, with histological analysis as the reference standard.	Slope and AUC were two best perfusion parameters to predict the severity of liver fibrosis ($>F2$ vs. $\leq F2$). Four significantly different variables were found between non-fibrotic versus mild-fibrotic subgroups: F (a), ART, Slope, and AUC; the best predictor for mild fibrosis was F (a) (AUROC:0.701).	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
65. Patel J, Sigmund EE, Rusinek H, Oei M, Babb JS, Taouli B. Diagnosis of cirrhosis with intravoxel incoherent motion diffusion MRI and dynamic contrast-enhanced MRI alone and in combination: preliminary experience. <i>J Magn Reson Imaging</i> . 2010;31(3):589-600.	Observational-Dx	14 patients with cirrhosis and 16 without cirrhosis.	To report our preliminary experience with the use of intravoxel incoherent motion (IVIM) diffusion-weighted magnetic resonance imaging (DW-MRI) and dynamic contrast-enhanced (DCE)-MRI alone and in combination for the diagnosis of liver cirrhosis.	PF, D*, D, and ADC values were significantly lower in cirrhosis (P = 0.0056-0.0377), whereas TTP, DV, and MTT were significantly increased in cirrhosis (P = 0.0006-0.0154). There was no correlation between IVIM- and DCE-MRI parameters. The highest Az (areas under the curves) values were observed for ADC (0.808) and TTP-DV (0.952 for each). The combination of ADC with DV and TTP provided 84.6% sensitivity and 100% specificity for diagnosis of cirrhosis.	3
66. Shah TU, Semelka RC, Pamuklar E, et al. The risk of hepatocellular carcinoma in cirrhotic patients with small liver nodules on MRI. <i>Am J Gastroenterol</i> . 2006;101(3):533-540.	Review/Other-Dx	310 liver transplant candidates.	To determine the risk of HCC in cirrhotic patients with small liver nodules on MRI compared to those without nodules.	A total of 310 liver transplant candidates with a mean follow-up of 663 days were included in the study and 133 underwent liver transplant during follow-up. The 1-yr incidence of HCC in the liver nodule group and control group was 11% and 0.5%, respectively, p < 0.001. The adjusted risk for HCC in the liver nodule group was 25 times higher compared to the control group, HR = 25.1 [95% CI 8.0, 78.9]. In 133 candidates who underwent transplant with and without liver nodules the rate of HCC was 11 (50%) and 4 (3.6%), respectively, p < 0.001.	4
67. Singal AG, Pillai A, Tiro J. Early detection, curative treatment, and survival rates for hepatocellular carcinoma surveillance in patients with cirrhosis: a meta-analysis. <i>PLoS Med</i> . 2014;11(4):e1001624.	Meta-analysis	47 studies with 15,158 patients.	To determine the effect of HCC surveillance on early stage tumor detection, receipt of curative therapy, and overall survival in patients with cirrhosis.	We identified 47 studies with 15,158 patients, of whom 6,284 (41.4%) had HCC detected by surveillance. HCC surveillance was associated with improved early stage detection (odds ratio [OR] 2.08, 95% CI 1.80-2.37) and curative treatment rates (OR 2.24, 95% CI 1.99-2.52). HCC surveillance was associated with significantly prolonged survival (OR 1.90, 95% CI 1.67-2.17), which remained significant in the subset of studies adjusting for lead-time bias. Limitations of current data included many studies having insufficient duration of follow-up to assess survival and the majority not adjusting for liver function or lead-time bias	M

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Gaba RC, Kallwitz ER, Parvinian A, et al. Imaging surveillance and multidisciplinary review improves curative therapy access and survival in HCC patients. <i>Ann Hepatol.</i> 2013;12(5):766-773.	Observational-Dx	167 patients	To evaluate the impact of HCC surveillance on use of curative therapies and survival in a region with long transplant waiting times.	58% of subjects underwent surveillance and MDC review of HCC. These patients were more likely to have received treatment with ablation or resection (16 vs. 3%, $P = 0.006$) and transplantation (23 vs. 4%, $P = 0.001$), and were less likely to develop tumor progression (45 vs. 68%, $P = 0.005$) or metastases (0 vs. 19%, $P < 0.001$). In multivariate analysis, surveillance and MDC review ($P = 0.034$, HR 0.520, 95% CI 0.284-0.952), tumor meeting Milan criteria ($P < 0.001$, HR 0.329, 95% CI 0.178-0.607), curative therapy application ($P = 0.048$, HR 0.130, 95% CI 0.017-0.979), and transplantation ($P = 0.004$, HR 0.236, 95% CI 0.088-0.632) were associated with survival.	3
69. El-Serag HB, Kramer JR, Chen GJ, Duan Z, Richardson PA, Davila JA. Effectiveness of AFP and ultrasound tests on hepatocellular carcinoma mortality in HCV-infected patients in the USA. <i>Gut.</i> 2011;60(7):992-997.	Observational-Dx	1480 HCV-infected patients.	To evaluate the effectiveness of HCC surveillance in a national Veterans Administration (VA) practice setting, using the national VA hepatitis C virus (HCV) Clinical Case Registry.	The mean survival was 1.8 years following the HCC diagnosis date. Surveillance AFP or US were recorded in 77.8% of patients within 2 years prior to HCC diagnosis. Annual surveillance with both AFP and US was observed in only 2% of patients. The presence of either AFP or US surveillance during both 0-6 month and 7-24 month periods before HCC diagnosis was associated with a lower mortality risk (HR 0.71, 95% CI 0.62 to 0.82) compared with no surveillance. Receipt of two or more surveillance tests in the 0-6 months (HR 0.76 95% CI 0.66 to 0.88) and to a lesser extent in the 7-12 months (HR 0.81 95% CI 0.1 to 0.99) prior to HCC diagnosis was also associated with reduced mortality risk.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
70. Wong GL, Wong VW, Tan GM, et al. Surveillance programme for hepatocellular carcinoma improves the survival of patients with chronic viral hepatitis. <i>Liver Int.</i> 2008;28(1):79-87.	Observational-Dx	579 patients	To examine the survival benefit of HCC surveillance in chronic viral hepatitis.	Among 579 patients (91% hepatitis B), 472 (82%) patients had HCC and 79 (17%) of these patients were referred from the surveillance programme. HCC was smaller (4.2 vs. 7.7 cm; $P<0.001$) and fewer in numbers (2.6 vs. 3.8, $P=0.03$) in the surveillance group vs. the no-surveillance group. Treatment by surgery (20 vs. 10%, $P=0.007$) and local ablative therapy (46 vs. 19%, $P<0.001$) were more frequent in the surveillance group than that in the no-surveillance group. The median survival of the surveillance group (88 weeks) was significantly longer than that of the no-surveillance group (26 weeks) ($P<0.001$). The adjusted cumulative survival at 2 years was significantly longer in the surveillance group if the tumour volume doubling time was <90 days ($P=0.0352$).	3
71. Stravitz RT, Heuman DM, Chand N, et al. Surveillance for hepatocellular carcinoma in patients with cirrhosis improves outcome. <i>Am J Med.</i> 2008;121(2):119-126.	Observational-Dx	269 patients	To assess whether the quality of surveillance for hepatocellular carcinoma influences prognosis by affecting access to liver transplantation.	Three-year survival in the 60 patients who underwent liver transplantation was 81% versus 12% for patients who did not undergo transplantation ($P<.001$). The percentages of patients who underwent transplantation according to tumor stage at diagnosis (T1, T2, T3, and T4) were 58%, 35%, 10%, and 1%, respectively. Hepatocellular carcinoma was diagnosed at stages 1 and 2 in 70% of patients in group 1, 37% of patients in group 2, and only 18% of patients in group 3 ($P<.001$). Liver transplantation was performed in 32% of patients in group 1, 13% of patients in group 2, and 7% of patients in group 3 ($P<.001$). Three-year survival from cancer diagnosis in patients in group 3 (12%) was significantly worse than in patients in group 1 (39%) or group 2 (27%) (each $P<.05$). Eighty percent of patients in group 3 had subtle abnormalities of cirrhosis on routine laboratory tests.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
72. Wald C, Russo MW, Heimbach JK, Hussain HK, Pomfret EA, Bruix J. New OPTN/UNOS policy for liver transplant allocation: standardization of liver imaging, diagnosis, classification, and reporting of hepatocellular carcinoma. <i>Radiology</i> . 2013;266(2):376-382.	Review/Other-Dx	N/A	To explain new policies on how imaging studies in these patients must be conducted and how findings must be reported.	A new liver allocation policy featuring improved imaging criteria for HCC exceptions has been developed and approved by OPTN/UNOS in late 2011. Included are minimum technical and protocol requirements for CT and MR imaging, diagnostic and classification criteria for HCC, and standardized reporting requirements.	4
73. U.S. Department of Health & Human Services. Organ Procurement and Transplantation Network. Policy 9. https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf#nameddest=Policy_09 .	Review/Other-Tx	N/A	To detail Organ Procurement and Transplantation Network policies.	No results stated in abstract.	4
74. Bolondi L, Gaiani S, Celli N, et al. Characterization of small nodules in cirrhosis by assessment of vascularity: the problem of hypovascular hepatocellular carcinoma. <i>Hepatology</i> . 2005; 42(1):27-34.	Observational-Dx	59 patients 72 lesions	Prospective study to look at the impact of arterial hypervascularity as a criterion for characterizing small (1-3 cm) nodules in cirrhosis.	Relying on imaging techniques in nodules of 1 to 2 cm would miss the diagnosis of HCC in up to 38% of cases. Any nodule >2 cm should be regarded as highly suspicious for HCC.	3
75. Choi JY, Lee JM, Sirlin CB. CT and MR imaging diagnosis and staging of hepatocellular carcinoma: part II. Extracellular agents, hepatobiliary agents, and ancillary imaging features. <i>Radiology</i> . 2014;273(1):30-50.	Review/Other-Dx	N/A	To discuss basic concepts of diagnosis and staging, reviews the diagnostic performance of CT and MR imaging with extracellular contrast agents and of MR imaging with hepatobiliary contrast agents, and examines in depth the major and ancillary imaging features used in the diagnosis and characterization of HCC.	No results stated in abstract.	4
76. Forner A, Reig M, Bruix J. Alpha-fetoprotein for hepatocellular carcinoma diagnosis: the demise of a brilliant star. <i>Gastroenterology</i> . 2009;137(1):26-29.	Review/Other-Dx	N/A	To evaluate usefulness of Alpha-fetoprotein (AFP) in the detection of HCC in the wake of the development of imaging techniques that have allowed the detection of HCC at an early stage.	No results stated in abstract.	4
77. Perkins JD. Seeding risk following percutaneous approach to hepatocellular carcinoma. <i>Liver Transpl</i> . 2007;13(11):1603.	Meta-analysis	99 articles	To evaluate the risk of seeding, defined as new neoplastic disease occurring outside the liver capsule, either in the subcutaneous tissue or peritoneal cavity following needle biopsy and/or local ablation therapy (LAT).	In 41 papers specifying the total number of patients biopsied and/or treated, the median risk of seeding was 2.29% (range 0-11%) for biopsy group; 1.4% (1.15-1.85%) for PEI when used with biopsy and 0.61% (0-5.56%) for RFA without biopsy, 0.95% (0-12.5%) for RFA with biopsy and 0.72% (0-10%) for liver nodules (including non-HCC nodules) biopsied and ablated.	M

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
78. American College of Radiology. Liver Imaging Reporting and Data System (LI-RADS). http://www.acr.org/quality-safety/resources/LIRADS .	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for Chronic Liver Disease.	N/A	4
79. American College of Radiology. ACR Appropriateness Criteria®: Liver Lesion — Initial Characterization. Available at: https://acsearch.acr.org/docs/69472/Narrative/ .	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for the initial characterization of liver lesions.	No results stated in abstract.	4
80. Forner A, Vilana R, Ayuso C, et al. Diagnosis of hepatic nodules 20 mm or smaller in cirrhosis: Prospective validation of the noninvasive diagnostic criteria for hepatocellular carcinoma. <i>Hepatology</i> . 2008;47(1):97-104.	Experimental-Dx	89 patients Note: CEUS was performed. T1 and T2 weighted MRI as well as contrast enhance MRI performed.	To evaluate the accuracy of contrast-enhanced ultrasound (CEUS) and MRI for the diagnosis of solitary nodules of 20 mm or smaller detected during surveillance in patients with cirrhosis	Final diagnoses were: HCC (n = 60), cholangiocarcinoma (n = 1), and benign lesions (regenerative/dysplastic nodule, hemangioma, focal nodular hyperplasia) (n = 28). Sex, cirrhosis cause, liver function, and alpha-fetoprotein (AFP) levels were similar between HCC and non-HCC groups. HCC patients were older and their nodules significantly larger (P < 0.0001). First biopsy was positive in 42 of 60 HCC patients. Sensitivity, specificity, and positive and negative predictive values of conclusive profile were 61.7%, 96.6%, 97.4%, and 54.9%, for MRI, 51.7%, 93.1%, 93.9%, and 50.9%, for CEUS. Values for coincidental conclusive findings in both techniques were 33.3%, 100%, 100%, and 42%. Thus, diagnosis of HCC 20 mm or smaller can be established without a positive biopsy if both CEUS and MRI are conclusive. However, sensitivity of these noninvasive criteria is 33% and, as occurs with biopsy, absence of a conclusive pattern does not rule out malignancy.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
81. Singal A, Volk ML, Waljee A, et al. Meta-analysis: surveillance with ultrasound for early-stage hepatocellular carcinoma in patients with cirrhosis. <i>Aliment Pharmacol Ther.</i> 2009;30(1):37-47.	Meta-analysis	13 Studies	To determine the performance characteristics of surveillance with ultrasound for the detection of HCC, particularly early HCC as defined by the Milan criteria.	Surveillance ultrasound detected the majority of tumours before they presented clinically, with a pooled sensitivity of 94%. However, ultrasound was less effective for detecting early HCC with a sensitivity of 63%. Alpha-fetoprotein provided no additional benefit to ultrasound. Meta-regression analysis demonstrated a significantly higher sensitivity for early HCC with ultrasound every 6 months than with annual surveillance. Current studies have limitations such as verification bias and are of suboptimal quality.	M
82. Gonzalez SA, Keeffe EB. Diagnosis of hepatocellular carcinoma: role of tumor markers and liver biopsy. <i>Clin Liver Dis.</i> 2011;15(2):297-306, vii-x.	Review/Other-Dx	N/A	To evaluate the role of tumor markers and liver biopsy in the diagnosis of hepatocellular carcinoma.	No results stated in abstract.	4
83. Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. <i>J Cancer Res Clin Oncol.</i> 2004;130(7):417-422.	Experimental-Dx	18,816 subjects	To assess the effect of screening on HCC mortality in people at increased risk.	The screened group completed 58.2 percent of the screening offered. When the screening group was compared to 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%CI 0.41-0.98).	1
84. Taouli B, Krinsky GA. Diagnostic imaging of hepatocellular carcinoma in patients with cirrhosis before liver transplantation. <i>Liver Transpl.</i> 2006;12(11 Suppl 2):S1-7.	Review/Other-Dx	N/A	To describe different imaging modalities used to evaluate hepatocellular carcinoma in patients with cirrhosis before liver transplantation.	No results stated in abstract.	4
85. Finberg HJ. Whither (with?) the ultrasound specialist? <i>J Ultrasound Med.</i> 2004;23(12):1543-1547.	Review/Other-Dx	N/A	To discuss the aspects of ultrasound that make it unique among diagnostic imaging modalities.	No results stated in abstract.	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
86. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. <i>J Hepatol.</i> 2012;56(4):908-943.	Review/Other-Tx	N/A	EASL–EORTC Clinical Practice Guidelines on the management of HCC.	n/a	4
87. Kudo M. Real practice of hepatocellular carcinoma in Japan: conclusions of the Japan Society of Hepatology 2009 Kobe Congress. <i>Oncology.</i> 2010;78 Suppl 1:180-188.	Review/Other-Dx	N/A	To present the current consensus on the management of hepatocellular carcinoma (HCC) formed at the 45th Annual Meeting of the Japan Society of Hepatology (June 4-5, 2009) and the 3rd International Kobe Liver Symposium (June 6-7, 2009) held in Kobe.	(1) Patients with type B or type C liver cirrhosis, who are an ultrahigh-risk group of liver cancer, should be screened every 3-4 months by ultrasonography and measurement of AFP and PIVKA-II. (2) Gd-EOB-MRI is useful for the diagnosis of early HCC. (3) The JIS score is more useful for the staging of liver cancer than the BCLC staging system, which is a global standard. (4) The TNM staging system by the Liver Cancer Study Group of Japan is superior to the TNM stage by the AJCC/UICC. (5) The therapeutic algorithm in the Japanese guidelines for the management of liver cancer is superior to the BCLC treatment algorithm. (6) Early stage. Liver cancers should be treated by radiofrequency ablation if they are ≤ 2 cm, and by surgical resection if they are Child-Pugh A solitary lesions. (7) Liver transplantation is only indicated for Child-Pugh C patients within Milan Criteria.	4
88. Omata M, Lesmana LA, Tateishi R, et al. Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma. <i>Hepatol Int.</i> 2010;4(2):439-474.	Review/Other-Tx	N/A	To develop consensus recommendations on the management of hepatocellular carcinoma.	Participants of the consensus meeting assessed the quality of cited studies and assigned grades to the recommendation statements. Finalized recommendations were presented at the fourth APASL single topic conference on viral-related HCC at Bali, Indonesia and approved by the participants of the conference.	4
89. Choi JY, Lee JM, Sirlin CB. CT and MR imaging diagnosis and staging of hepatocellular carcinoma: part I. Development, growth, and spread: key pathologic and imaging aspects. <i>Radiology.</i> 2014;272(3):635-654.	Review/Other-Dx	N/A	To discuss the current state of the art for the imaging-based diagnosis and staging of HCC, focusing on CT and MR imaging, as these are the most commonly used modalities for these purposes.	No results stated in abstract.	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
90. Kim KA, Kim MJ, Choi JY, Chung YE. Development of hepatocellular carcinomas in patients with absence of tumors on a prior ultrasound examination. <i>Eur J Radiol.</i> 2012;81(7):1450-1454.	Review/Other-Dx	100 patients	To evaluate hepatocellular carcinoma (HCC) that developed in patients with no evidence of a tumor during a prior ultrasound (US) performed within 1 year of the diagnosis.	The mean interval between the negative and diagnostic scans was 5 months, 13 days. HCC presented as a single nodule in 69 patients (size, 0.8-8.0 cm), as two or more nodules in 18 patients, and as the diffuse form of HCC in 13 patients. HCC presented as a small tumor (<3 cm) in 48 patients. T stages were: T1 in 26 patients, T2 in 45, T3 in 18, and T4 in 11. The Milan criteria were met in 79 patients. Eighty-five patients fulfilled the UCSF.	4
91. Yu NC, Chaudhari V, Raman SS, et al. CT and MRI improve detection of hepatocellular carcinoma, compared with ultrasound alone, in patients with cirrhosis. <i>Clin Gastroenterol Hepatol.</i> 2011;9(2):161-167.	Observational-Dx	638 patients with cirrhosis	To analyze the ability of ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) to detect HCC.	Of the 638 patients, 225 (35%) had HCC, confirmed by pathology analysis of liver explants. In 23 cases, the lesions were infiltrative or extensively multifocal. In the remaining 202 explants (337 numerable, discrete nodules), respective lesion-based sensitivities of US, CT, and MRI were 46%, 65%, and 72% overall and 21%, 40%, and 47% for small (<2 cm) HCC. The sensitivity of US increased with the availability of CT or MRI data (P = .049); sensitivity values were 62% and 85% for lesions 2-4 and >= 4 cm, respectively. Patient-based specificities of US, CT, and MRI were 96%, 96%, and 87%, respectively.	3
92. Singal AG, Conjeevaram HS, Volk ML, et al. Effectiveness of hepatocellular carcinoma surveillance in patients with cirrhosis. <i>Cancer Epidemiol Biomarkers Prev.</i> 2012;21(5):793-799.	Observational-Dx	446 patients	To evaluate the effectiveness of a surveillance program with ultrasound and alpha-fetoprotein (AFP) to detect early HCCs.	After a median follow-up of 3.5 years, 41 patients developed HCCs, of whom 30 (73.2%) had early HCCs. The annual incidence of HCC was 2.8%, with cumulative 3- and 5-year incidence rates of 5.7% and 9.1%, respectively. Surveillance ultrasound and AFP had sensitivities of 44% and 66% and specificities of 92% and 91%, respectively, for the detection of HCCs. Sensitivity significantly improved to 90%, with minimal loss in specificity (83%) when these tests were used in combination.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
93. Colli A, Fraquelli M, Casazza G, et al. Accuracy of ultrasonography, spiral CT, magnetic resonance, and alpha-fetoprotein in diagnosing hepatocellular carcinoma: a systematic review. <i>Am J Gastroenterol.</i> 2006;101(3):513-523.	Meta-analysis	14 studies	To systematically assess the accuracy of ultrasound scan (US), spiral computed tomography (CT), magnetic resonance imaging (MRI), and alpha-fetoprotein (AFP) in diagnosing hepatocellular carcinoma (HCC).	The pooled estimates of the 14 US studies were 60% (95% CI 44-76) for sensitivity, 97% (95% CI 95-98) for specificity, 18 (95% CI 8-37) for LR+, and 0.5 (95% CI 0.4-0.6) for LR-; for the 10 CT studies sensitivity was 68% (95% CI 55-80), specificity 93% (95% CI 89-96), LR+ 6 (95% CI 3-12), and LR- 0.4 (95% CI 0.3-0.6); for the nine MRI studies sensitivity was 81% (95% CI 70-91), specificity 85% (95% CI 77-93), LR+ 3.9 (95% CI 2-7), and LR- 0.3 (95% CI 0.2-0.5). The sensitivity and specificity of AFP varied widely, and this could not be entirely attributed to the threshold effect of the different cutoff levels used.	M
94. Jang HJ, Kim TK, Wilson SR. Small nodules (1-2 cm) in liver cirrhosis: characterization with contrast-enhanced ultrasound. <i>Eur J Radiol.</i> 2009; 72(3):418-424.	Observational-Dx	59 patients	To determine the diagnostic efficacy of arterial phase CEUS for characterizing small hepatic nodules (1-2 cm) in patients with high-risk for HCC.	At the time of CEUS, the 59 nodules were diagnosed as HCC in 26 and benign lesions in 33, including 20 regenerative nodules/DN, 11 hemangiomas, and 2 focal fat sparing. All 26 nodules with arterial phase hypervascularity without hemangioma-like features were HCC. However, CEUS misdiagnosed HCC as regenerative nodules/DN in 4 cases with arterial iso- (n=3) or hypovascularity (n=1). CEUS correctly diagnosed all 11 hemangiomas. The sensitivity, specificity, and accuracy of CEUS for diagnosing HCC were 86.7%, 100%, and 93.2%.	3
95. D'Onofrio M, Faccioli N, Zamboni G, et al. Focal liver lesions in cirrhosis: value of contrast-enhanced ultrasonography compared with Doppler ultrasound and alpha-fetoprotein levels. <i>Radiol Med.</i> 2008;113(7):978-991.	Observational-Dx	128 cirrhotic patients Note: Contrast enhanced ultrasound performed.	To evaluate the diagnostic value of contrast-enhanced ultrasound (CEUS) in characterising focal liver lesions in cirrhosis and to validate its use in lesions discovered during surveillance for hepatocellular carcinoma (HCC).	A total of 207 focal liver lesions (101 benign and 106 malignant) were identified in 128 patients. CEUS sensitivity and specificity for lesion characterisation were 96.2% and 97.0%, respectively, whereas its positive and negative predictive values were 97.1% and 96.1%. CEUS accuracy was 96.6%, higher than that of US (72.0%), Doppler US (70.0%), AFP levels (65.7%), combined US and Doppler US (70.0%) and combined US and AFP levels (90.3%). The differences between US and CEUS were statistically significant (p<0.05).	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
96. Wang JH, Lu SN, Hung CH, et al. Small hepatic nodules (< or =2 cm) in cirrhosis patients: characterization with contrast-enhanced ultrasonography. Liver Int. 2006;26(8):928-934.	Observational-Dx	30 cirrhosis patients	To evaluate the efficacy of contrast-enhanced ultrasonography (CEUS) for the characterization of small hepatic nodules (< or =2 cm) in cirrhosis patients.	CEUS showed AE in 15 nodules (13 HCC and two benign) and ADE in 17 lesions (14 HCC and three benign). For HCC, the coincidental AE of both CEUS and dynamic CT was 40%. Using both AE and ADE for HCC diagnosis, the sensitivity, specificity, accuracy, positive predictive value and negative predictive values were 55.6%, 91.7%, 70%, 90.9% and 57.9%, respectively. When using either AE or ADE for HCC diagnosis, the same parameters were 94.4%, 66.7%, 83.3%, 81% and 88.9%, respectively. One benign hepatic nodule with both AE and ADE was diagnosed as HCC 29 months after the CEUS study.	3
97. Xu HX, Lu MD, Liu LN, et al. Discrimination between neoplastic and non-neoplastic lesions in cirrhotic liver using contrast-enhanced ultrasound. Br J Radiol. 2012;85(1018):1376-1384.	Observational-Dx	133 cirrhotic patients	To assess the value of contrast-enhanced ultrasound (CEUS) in differentiating hepatocellular carcinoma (HCC) from non-neoplastic lesion in cirrhotic liver in comparison with baseline ultrasound.	Hypervascularity was observed in 94.8% (110/116) HCCs, 3.8% (1/26) macroregenerative nodules and 60.0% (3/5) high-grade dysplastic nodules during arterial phase on CEUS. Detection rates of typical vascular pattern (i.e. hypervascularity during arterial phase and subsequent washout) in HCCs with a diameter of $\leq 2.0\text{ cm}$, 2.1-3.0 cm and 3.1-5.0 cm were 69.2% (27/39), 97.1% (33/34) and 100.0% (43/43), respectively. CEUS significantly improved the sensitivity [88.8% (103/116) vs 37.1% (43/116), $p < 0.001$], negative predictive value [70.5% (31/44) vs 31.5% (29/92), $p < 0.001$], and accuracy [91.2% (134/147) vs 49.0% (72/147), $p < 0.001$] in differentiating HCCs from non-neoplastic lesions when compared with baseline ultrasound. However, the sensitivity and accuracy of CEUS for HCCs $\leq 2.0\text{ cm}$ in diameter were significantly lower than those for HCCs of 2.1-3.0 cm and 3.1-5.0 cm in diameter.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
98. Claudon M, Dietrich CF, Choi BI, et al. Guidelines and good clinical practice recommendations for Contrast Enhanced Ultrasound (CEUS) in the liver - update 2012: A WFUMB-EFSUMB initiative in cooperation with representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS. <i>Ultrasound Med Biol.</i> 2013;39(2):187-210.	Review/Other-Dx	N/A	To provide general advice on the use of all currently clinically available ultrasound contrast agents (UCA).	No results stated in abstract.	4
99. Khalili K, Kim TK, Jang HJ, et al. Optimization of imaging diagnosis of 1-2 cm hepatocellular carcinoma: an analysis of diagnostic performance and resource utilization. <i>J Hepatol.</i> 2011;54(4):723-728.	Observational-Dx	84 cirrhotic patients Note: Contrast Enhanced Ultrasound, 4-phase CT, and T1 and T2 weighted images, and 3D fluoro-triggered MRI performed.	To determine the optimal imaging scan or combinations in terms of diagnostic performance and resource utilization for 1-2 cm nodules found on surveillance for hepatocellular carcinoma.	For single imaging scans, sensitivities/specificities ranged between 53-62% and 91-100%. When two scans were combined requiring both to be positive, sensitivities/specificities ranged between 29-41% and 99-100%. When two scans were combined sequentially, requiring only one to be positive, sensitivities/specificities ranged between 74-89% and 91-99%. When comparing combination of two positive tests (MRI and CT) to MRI alone, there was a significant drop in sensitivity (41% vs. 62%, p=0.02), no change in specificity (both 100%), with twice as many scans performed, and 9% rise in potential biopsies or 7% rise in follow-up scans. When comparing the combination of MRI then CT (if MRI negative) to MRI alone, there was an insignificant rise in sensitivity (74% vs. 62%, p=0.13), drop in specificity (97% vs. 100%), with 77% more scans performed, and 6% drop in potential biopsies or 7% drop in potential follow-up scans	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
100. Sangiovanni A, Manini MA, Iavarone M, et al. The diagnostic and economic impact of contrast imaging techniques in the diagnosis of small hepatocellular carcinoma in cirrhosis. <i>Gut</i> . 2010;59(5):638-644.	Observational-Dx	64 patients Note: Contrast enhanced ultrasound, CT and MRI were performed.	To assess the sensitivity, specificity, diagnostic accuracy and economic impact of all possible sequential combinations of contrast imaging techniques in patients with cirrhosis with 1-2 cm liver nodules undergoing US surveillance.	HCC was diagnosed in 44 (66%) nodules (2, <1 cm; 34, 1-2 cm; 8, >2 cm). The sensitivity of CE-US, CT and MRI for 1-2 cm HCC was 26, 44 and 44%, with 100% specificity, the typical vascular pattern of HCC being identified in 22 (65%) by a single technique versus 12 (35%) by at least two techniques carried out at the same time point (p=0.028). Compared with the cheapest dual examination (CE-US+CT), the cheapest single technique of stepwise imaging diagnosis of HCC was equally expensive (euro 26 440 vs euro 28 667), but led to a 23% reduction of FNB procedures (p=0.031).	2
101. Kim TK, Lee KH, Jang HJ, et al. Analysis of gadobenate dimeglumine-enhanced MR findings for characterizing small (1-2-cm) hepatic nodules in patients at high risk for hepatocellular carcinoma. <i>Radiology</i> . 2011;259(3):730-738.	Observational-Dx	96 patients	To retrospectively identify magnetic resonance (MR) imaging findings that are associated with hepatocellular carcinoma (HCC) in 1-2-cm nodules detected at surveillance ultrasonography (US) and to propose newer MR imaging diagnostic criteria.	Univariate analysis revealed four imaging findings associated with HCC, including arterial phase hyperintensity, portal or delayed phase hypointensity (washout), hyperintensity on T2-weighted images, and hepatobiliary phase hypointensity (P < .001 for each). In the multivariable analysis, arterial phase hyperintensity (adjusted odds ratio [OR], 17.1; P = .003) and washout (adjusted OR, 11.7; P = .007) were associated with HCC. Of the developed criteria, the criteria including nodules fitting the AASLD practice guideline (arterial phase hyperintensity and washout) or nodules having three or more findings were considered most reasonable, showing improved sensitivity (77% [33 of 43] versus 67% [29 of 43], P = .048) and comparable specificity (95% [69 of 73] versus 99% [72 of 73], P = .09), as compared with AASLD practice guideline.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
102. Rimola J, Forner A, Tremosini S, et al. Non-invasive diagnosis of hepatocellular carcinoma \leq 2 cm in cirrhosis. Diagnostic accuracy assessing fat, capsule and signal intensity at dynamic MRI. J Hepatol. 2012;56(6):1317-1323.	Observational-Dx	159 patients Note: Contrast enhanced ultrasound performed	To assess the diagnostic accuracy of the incorporation of additional magnetic resonance imaging (MRI) parameters in those based on contrast enhancement pattern for the diagnosis of solitary nodules between 5 and 20mm, detected during surveillance in patients with cirrhosis.	Final diagnoses were hepatocellular carcinoma (HCC) (n=103), other malignant lesions (intrahepatic cholangiocarcinoma/metastases) (n=4), and benign lesions (n=52). The specific enhancement pattern (arterial enhancement followed by washout) yielded a sensitivity and specificity of 58.3% and 96.4%, respectively. Peritumoral capsule was present in 43 HCC and in 2 non-HCC lesions. Intralesional fat was detected in 24 nodules; 5 nodules were non-HCC. Finally, the presence of both capsule and fat was observed in 10 cases, all of them HCC (100% specificity), but all of them also displayed the specific enhancement pattern, thus adding no sensitivity or specificity.	2
103. Akai H, Kiryu S, Matsuda I, et al. Detection of hepatocellular carcinoma by Gd-EOB-DTPA-enhanced liver MRI: comparison with triple phase 64 detector row helical CT. Eur J Radiol. 2011;80(2):310-315.	Observational-Dx	34 patients Note: Contrast Enhanced MRI performed as well as CT without and with contrast (multiphasic study).	To compare the diagnostic performance of Gd-EOB-DTPA-enhanced MRI with that of triple phase 64-MDCT in the detection of hepatocellular carcinoma (HCC).	Both observers showed higher sensitivity in detecting lesions with MRI compared to CT, however, only the difference between the two imaging techniques for observer 2 was significant (P=0.034). For lesions 1cm or smaller, MRI and CT showed equal sensitivity (both 62.5%) with one observer, and MRI proved superior to CT with the other observer (MRI 75% vs. CT 56.3%), but the latter difference was not significant (P=0.083). The difference in positive and negative predictive value between the two imaging techniques for each observer was not significant (P>0.05). The areas under the ROC curve for each observer were 0.843 and 0.861 for MRI vs. 0.800 and 0.833 for CT and the differences were not significant. Reproducibility was higher using MRI for both observers, but the result was not significant (MRI 32/33 vs. CT 29/33, P=0.083).	1

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
104. Inoue T, Kudo M, Komuta M, et al. Assessment of Gd-EOB-DTPA-enhanced MRI for HCC and dysplastic nodules and comparison of detection sensitivity versus MDCT. <i>J Gastroenterol.</i> 2012;47(9):1036-1047.	Observational-Dx	66 patients with 86 nodules	To evaluate gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance imaging (MRI) for the detection of hepatocellular carcinomas (HCCs) and dysplastic nodules (DNs) compared with dynamic multi-detector row computed tomography (MDCT), and to discriminate between HCCs and DNs.	For hypervascular HCCs, the diagnostic ability of Gd-EOB-DTPA-enhanced MRI was significantly higher than that of MDCT for tumors less than 2 cm (p = 0.048). There was no difference in the detection of hypervascular HCCs between hepatobiliary phase images of Gd-EOB-DTPA-enhanced MRI (43/45: 96%) and dynamic MDCT (40/45: 89%), whereas the detection sensitivity of hypovascular tumors by Gd-EOB-DTPA-enhanced MRI was significantly higher than that by dynamic MDCT (39/41: 95% vs. 25/41: 61%, p = 0.001). EOB enhancement ratios were decreased in parallel with the degree of differentiation in DN and HCCs, although there was no difference between DN and hypovascular well-differentiated HCCs.	2
105. Marrero JA, Hussain HK, Nghiem HV, Umar R, Fontana RJ, Lok AS. Improving the prediction of hepatocellular carcinoma in cirrhotic patients with an arterially-enhancing liver mass. <i>Liver Transpl.</i> 2005;11(3):281-289.	Observational-Dx	94 patients	To determine whether clinical, laboratory, and / or radiologic data can improve the prediction of HCC in cirrhotic patients with an arterially-enhancing mass.	Delayed hypointensity of an arterially-enhancing mass had a sensitivity of 89% and a specificity of 96% for HCC. The presence of delayed hypointensity was the only independent predictor of HCC among patients with arterially-enhancing lesions <2 cm (odds ratio, 6.3; 95% confidence interval [CI], 1.8-13), with a sensitivity of 80% and a specificity of 95%.	3
106. Ooka Y, Kanai F, Okabe S, et al. Gadoteric acid-enhanced MRI compared with CT during angiography in the diagnosis of hepatocellular carcinoma. <i>Magn Reson Imaging.</i> 2013;31(5):748-754.	Observational-Dx	54 patients	To assess the value of gadoteric acid-enhanced magnetic resonance imaging (MRI) for the pre-therapeutic detection of hepatocellular carcinoma (HCC) using receiver operating characteristic (ROC) analysis with the combination of computed tomography (CT) arterial portography and CT hepatic arteriography (CTAP/CTHA).	NOTE: Contrast enhanced CT and Contrast enhanced MRI performed. For each reader, the area under the curve was significantly higher for Set 2 than for Set 1. The mean area under the curve was also significantly greater for Set 2 than for Set 1 (area under the curve, 0.98 vs. 0.93; P=.0009). The sensitivity was significantly higher for Set 2 than for Set 1 for all three readers (P=.012, .013 and .039, respectively). The difference in	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
107. Rhee H, Kim MJ, Park MS, Kim KA. Differentiation of early hepatocellular carcinoma from benign hepatocellular nodules on gadoxetic acid-enhanced MRI. Br J Radiol. 2012;85(1018):e837-844.	Observational-Dx	34 patients	To test new diagnostic criteria for the discrimination of early hepatocellular carcinoma (HCC) from benign hepatocellular nodules on gadoxetic acid-enhanced MRI (Gd-EOB-MRI).	A size cut-off value (≥ 1.5 cm diameter) and MRI findings of T(1) hypointensity, T(2) hyperintensity, DWI hyperintensity on both low and high b-value images (b=50 and 800 s mm ⁻²), respectively), arterial enhancement, late washout and hepatobiliary hypointensity were selected as the diagnostic criteria. When lesions were considered malignant if they satisfied three or more of the above criteria, the sensitivity was significantly higher than when making a diagnosis based on arterial enhancement and washout alone (58.6% vs 13.8%, respectively; p=0.0002), while the specificity was 100.0% for both criteria.	2
108. Luca A, Caruso S, Milazzo M, et al. Multidetector-row computed tomography (MDCT) for the diagnosis of hepatocellular carcinoma in cirrhotic candidates for liver transplantation: prevalence of radiological vascular patterns and histological correlation with liver explants. Eur Radiol. 2010;20(4):898-907.	Observational-Dx	125 cirrhotic patients	To define the prevalence of different multidetector-row computed tomography (MDCT) vascular patterns and their histopathological correlation with liver explants, and to evaluate the accuracy of MDCT for the diagnosis of hepatocellular carcinoma (HCC).	Positive predictive value (PPV) and likelihood ratio (LR) were 95% and 18.66, respectively, for Hyper-L-Wo; 45% and 0.82 for Hyper-L; and 75% and 3 for Hypo-L of 20 mm or larger. Overall accuracy of MDCT for detection and characterisation of HCC was 89% and 43%, respectively. Sensitivity of MDCT for detection and characterisation was related to the lesion size, ranging from 78% (lesion smaller than 10 mm) to 98% (larger than 20 mm) and from 9% to 64%, respectively. MDCT established the accurate stage of disease in 46% of the patients, underestimated in 52% and overestimated in 2%.	3
109. Golfieri R, Renzulli M, Lucidi V, Corcioni B, Trevisani F, Bolondi L. Contribution of the hepatobiliary phase of Gd-EOB-DTPA-enhanced MRI to Dynamic MRI in the detection of hypovascular small (≤ 2 cm) HCC in cirrhosis. Eur Radiol. 2011;21(6):1233-1242.	Observational-Dx	127 cirrhotic patients. Note: Gd-EOB-DTPA-MRI performed as unenhanced and dynamic; unenhanced, dynamic and HB phases.	To prospectively assess the additional value of the hepatobiliary (HB) phase of Gd-EOB-DTPA-MRI in identifying and characterising small (≤ 2 cm) hepatocellular carcinomas (HCCs) undetermined in dynamic phases alone because of their atypical features, according to the AASLD criteria.	62 atypical nodules were reported at histology: high-grade dysplastic nodules (HGDN)/early HCC (n = 20), low-grade DN (LGDN) (n = 21), regenerative nodules (n = 17) and nodular regenerative hyperplasia (n = 4). The sensitivity, specificity, accuracy, positive and negative predictive value (PPV, NPV) were increased by the addition of the HB phase: 88.4-99.4%, 88-95%, 88-98.5%, 97-99%, and 65-97.5%, respectively. Twenty atypical nodules were malignant (32%), 19 of which were characterised only during the HB phase.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
110. Granito A, Galassi M, Piscaglia F, et al. Impact of gadoxetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance on the non-invasive diagnosis of small hepatocellular carcinoma: a prospective study. <i>Aliment Pharmacol Ther.</i> 2013;37(3):355-363.	Observational-Dx	33 patients. Note: Contrast enhanced US and MRI performed as well as quadruple-phase CT.	To evaluate the contribution of the hepatobiliary phase of Gd-EOB-DTPA MR in the diagnosis of small hepatocellular carcinoma (HCC) in cirrhotic patients under surveillance.	Of the 48 nodules, 38 (79%) were diagnosed as HCC, 24 (63%) of them based on AASLD non-invasive criteria, 11 diagnosed at histology and 3 during follow-up. The typical vascular pattern (arterial hypervascularisation and venous/late washout) was detected in 30 (79%) HCC nodules by MR, in 22 (58%) by CT and in 17 (45%) by CEUS. Hypointensity during the MR hepatobiliary phase was observed in all HCC nodules and in 3 nonmalignant nodules (sensitivity 100%, specificity 70%, positive predictive value 93%, negative predictive value 100%, positive likelihood ratio 3.33, negative likelihood ratio 0). Eight (21%) of the 38 HCC nodules, 7 of which lacked the typical vascular features at any of the imaging modalities, showed washout in the portal/venous phase and hypointensity in the hepatobiliary phase at MRI, while this pattern was not detected in any nonmalignant lesion.	2
111. Piana G, Trinquart L, Meskine N, Barrau V, Beers BV, Vilgrain V. New MR imaging criteria with a diffusion-weighted sequence for the diagnosis of hepatocellular carcinoma in chronic liver diseases. <i>J Hepatol.</i> 2011;55(1):126-132.	Observational-Dx	91 patients. Note: Contrast enhanced MRI with diffusion-weighted imaging.	To propose MRI criteria with a diffusion-weighted imaging (DWI) sequence for the diagnosis of hepatocellular carcinoma (HCC).	Ninety-one patients were included (109 HCCs). The sensitivity of conventional MRI criteria for the diagnosis of HCC was 59.6% for both radiologists. The sensitivity of enhancement in the arterial-dominant phase and hyperintensity on DWI was 77.1% or 76.1%, depending on the radiologist. The sensitivity of enhancement in the arterial-dominant phase and washout in the portal venous and/or equilibrium phases or hyperintensity on DWI was 84.4% or 85.3%, depending on the radiologist. The inter-observer agreement for the latter was very good (kappa coefficient 0.82). These results were consistent in HCCs smaller than 20mm.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
112. Sano K, Ichikawa T, Motosugi U, et al. Imaging study of early hepatocellular carcinoma: usefulness of gadoxetic acid-enhanced MR imaging. <i>Radiology</i> . 2011;261(3):834-844.	Observational-Dx	64 patients	To describe imaging findings of early hepatocellular carcinoma (HCC) at gadoxetic acid-enhanced magnetic resonance (MR) imaging, dynamic contrast material-enhanced computed tomography (CT), CT during arterial portography (CTAP), and CT during hepatic arteriography (CTHA) and to compare the diagnostic performance of each modality for small (≤ 2 cm) HCC.	The imaging features that are statistically significant for differentiating an early HCC from a DN include fat-containing lesions at dual-echo T1-weighted MR imaging (seen in 16 of the 30 early HCCs and none of the DNs), low attenuation at unenhanced CT (seen in 13 of the 30 early HCCs and none of the DNs), low attenuation at CTAP (seen in 11 of the 30 early HCCs and none of the DNs), and low signal intensity at hepatocyte phase gadoxetic acid-enhanced MR imaging (seen in 29 of the 30 early HCCs and none of the DNs). The diagnostic performance of gadoxetic acid-enhanced MR imaging (A(z), 0.98 and 0.99) was significantly greater than that of contrast-enhanced CT (A(z), 0.87) and CTHA-CTAP (A(z), 0.85 and 0.86) owing to its significantly higher sensitivity ($P < .001$).	3
113. Sun HY, Lee JM, Shin CI, et al. Gadoxetic acid-enhanced magnetic resonance imaging for differentiating small hepatocellular carcinomas ($< \text{or} = 2$ cm in diameter) from arterial enhancing pseudolesions: special emphasis on hepatobiliary phase imaging. <i>Invest Radiol</i> . 2010;45(2):96-103.	Observational-Dx	69 patients	To determine the characteristic enhancing features of hepatocellular carcinoma (HCC) and arterial-enhancing pseudolesion (AEP) on gadoxetic acid (Primovist)-enhanced magnetic resonance imaging (MRI) and to assess its performance compared with that of multirow detector computed tomography (MDCT) for differentiating small HCC ($< \text{or} = 2$ cm in diameter) from AEP in cirrhotic liver.	Among 44 HCCs, 42 (95.4%) demonstrated low signal intensity (SI) and only 2 showed iso- or high SI on the hepatobiliary phase of gadoxetic acid-enhanced MRI. Alternatively, most AEPs showed iso SI on the hepatobiliary ($n = 50$, 94.3%) phase, and only 2 AEPs showed low SI. Compared with the diagnostic performance of the 2 imaging modalities, the mean areas under the receiver-operator characteristic curves on MR imaging were 0.975 for reviewer 1 and 0.966 for reviewer 2, whereas those of CT imaging were 0.892 for reviewer 1 and 0.888 for reviewer 2 ($P = 0.069$ and $P = 0.106$, respectively). The sensitivity for each reviewer with MR imaging (93.9% and 90.9%, respectively) was significantly higher than that with multiphasic CT (54.5%, in both) ($P = 0.001$ and 0.0018, respectively).	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
114. Furlan A, Marin D, Vanzulli A, et al. Hepatocellular carcinoma in cirrhotic patients at multidetector CT: hepatic venous phase versus delayed phase for the detection of tumour washout. <i>Br J Radiol.</i> 2011;84(1001):403-412.	Observational-Dx	30 patients	To compare retrospectively hepatic venous and delayed phase images for the detection of tumour washout during multiphase multidetector row CT (MDCT) of the liver in patients with hepatocellular carcinoma (HCC).	48 HCCs were detected at MDCT. 46 of the 48 tumours (96%) appeared as either hyper- or isoattenuating during the hepatic arterial phase subjective washout was present in 15 HCCs (33%) during the hepatic venous phase and in 35 (76%) during the delayed phase ($p < 0.001$, McNemar's test). Objective washout was present in 30 of the 46 HCCs (65%) during the hepatic venous phase and in 42 of the HCCs (91%) during the delayed phase ($p = 0.001$). The delayed phase yielded significantly higher mean TLC absolute values compared with the hepatic venous phase (-16.1 \pm 10.8 HU vs -10.5 \pm 10.2 HU; $p < 0.001$).	2
115. Cereser L, Furlan A, Bagatto D, et al. Comparison of portal venous and delayed phases of gadolinium-enhanced magnetic resonance imaging study of cirrhotic liver for the detection of contrast washout of hypervascular hepatocellular carcinoma. <i>J Comput Assist Tomogr.</i> 2010;34(5):706-711.	Observational-Dx	33 patients. Note: MRI performed with and without contrast.	To retrospectively compare portal venous phase (PVP) and delayed phase (DP) for the detection of tumor washout at gadobenate dimeglumine-enhanced liver magnetic resonance imaging (MRI) in cirrhotic patients with hypervascular hepatocellular carcinoma (HCC).	Among 54 hypervascular HCCs, washout was present in 24 (44%) of 54 tumors on PVP and in 44 (82%) of 54 on DP ($P < 0.001$). In 20 (37%) of 54 tumors, washout was deemed present only on DP. Delayed phase images yielded significantly higher mean tumor-to-liver contrast absolute values compared with PVP images (-24.5 [56.1] vs -9.3 [52.6], $P = 0.001$).	2
116. Anzidei M, Di Martino M, Sacconi B, et al. Evaluation of image quality, radiation dose and diagnostic performance of dual-energy CT datasets in patients with hepatocellular carcinoma. <i>Clin Radiol.</i> 2015;70(9):966-973.	Observational-Dx	30 patients	To evaluate image quality and diagnostic accuracy of different dual-energy computed tomography (DECT) datasets for identification of hepatocellular carcinoma (HCC), assess the reliability of virtual unenhanced (VU) images in replacing standard unenhanced (SU) images, and quantify effective dose (ED) at different tube voltages.	Thirty-eight HCC and 18 benign lesions were detected at 80 kVp, 33 HCC and 22 benign lesions were detected at 140 kVp, and 36 HCC and 20 benign lesions were detected at mixed tube potentials. Final diagnosis confirmed 37 HCC and 20 benign lesions. There was no significant difference in diagnostic confidence between 80 kVp, 140 kVp, and mixed tube potential arterial datasets ($p > 0.05$). Image quality was adequate for all datasets, with increased quality at higher tube potential (80 versus 140 kVp, $p = 0.001$; mixed versus 140 kVp, $p = 0.001$; 80 kVp versus mixed, $p = 0.0024$). Significant ED reduction was observed between 140 and 80 kVp datasets ($p < 0.001$).	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
117. Hanna RF, Aguirre DA, Kased N, Emery SC, Peterson MR, Sirlin CB. Cirrhosis-associated hepatocellular nodules: correlation of histopathologic and MR imaging features. <i>Radiographics</i> . 2008;28(3):747-769.	Review/Other-Dx	N/A	To review the current classification of cirrhosis-associated hepatocellular nodules and survey the magnetic resonance (MR) imaging techniques that may be used to evaluate the cirrhotic liver.	Different categories of hepatocellular nodules have imaging characteristics that overlap considerably, a comprehensive familiarity with diagnostically specific features at unenhanced and contrast-enhanced MR imaging may help distinguish benign lesions from premalignant and malignant ones.	4
118. Loyer EM, Chin H, DuBrow RA, David CL, Eftekhari F, Charnsangavej C. Hepatocellular carcinoma and intrahepatic peripheral cholangiocarcinoma: enhancement patterns with quadruple phase helical CT--a comparative study. <i>Radiology</i> . 1999;212(3):866-875.	Observational-Dx	45 patients	To define the hemodynamic features of hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma by using quadruple phase helical computed tomography (CT) and determine the value of this information in characterizing tumors.	In the majority of HCC lesions, a single, early peak of enhancement followed by a continuous decrease in tumor attenuation over time was seen. The greatest tumor conspicuity occurred during the delayed phase. In cholangiocarcinoma, tumor attenuation increased during the delayed phase. In the majority of lesions, the greatest tumor conspicuity was seen during the portal venous phase. In both tumor types, the diagnostic confidence level improved when the delayed phase was used.	3
119. Doyle DJ, O'Malley ME, Jang HJ, Jhaveri K. Value of the unenhanced phase for detection of hepatocellular carcinomas 3 cm or less when performing multiphase computed tomography in patients with cirrhosis. <i>J Comput Assist Tomogr</i> . 2007;31(1):86-92.	Observational-Dx	36 patients. Note: Dual-phase CT with and without contrast performed.	To determine whether unenhanced images are of added benefit to dual-phase computed tomography (CT) for detection of hepatocellular carcinomas (HCCs) 3 cm or less.	For readers 1 and 2, unenhanced CT was subjectively helpful in 16 (5%) of 324 and 23 (7%) of 324 segments. Sensitivity and area under the receiver operating characteristic curve were identical for dual-phase versus triple-phase images for reader 1 (82.4% and 0.882) and reader 2 (100% and 0.997).	2
120. Iannaccone R, Laghi A, Catalano C, et al. Hepatocellular carcinoma: role of unenhanced and delayed phase multi-detector row helical CT in patients with cirrhosis. <i>Radiology</i> . 2005;234(2):460-467.	Observational-Dx	195 patients. Note: Quadruple-phase CT performed.	To determine, by using multi-detector row helical computed tomography (CT), the added value of obtaining unenhanced and delayed phase scans in addition to biphasic (hepatic arterial and portal venous phases) scans in the detection of hepatocellular carcinoma (HCC) in patients with cirrhosis.	Mean sensitivity and positive predictive values, respectively, for HCC detection were 88.8% (666 of 750 readings) and 97.8% (666 of 681 readings) for the combined hepatic arterial and portal venous phases, 89.2% (669 of 750 readings) and 97.8% (669 of 684 readings) for hepatic arterial and portal venous phases with the unenhanced phase, 92.8% (696 of 750 readings) and 97.3% (696 of 715 readings) for hepatic arterial and portal venous phases with the delayed phase, and 92.8% (696 of 750 readings) and 97.3% (696 of 715 readings) for all four phases combined. The reading sessions in which delayed phase images were available for interpretation showed significantly ($P < .05$) superior sensitivity and A(z) values.	2

* See Last Page for Key

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
121. Luke FE, Allen BC, Moshiri ST, et al. Multiphase multi-detector row computed tomography in the setting of chronic liver disease and orthotopic liver transplantation: can a series be eliminated in order to reduce radiation dose? J Comput Assist Tomogr. 2013;37(3):408-414.	Observational-Dx	140 patients	To explore utilization of multi-detector row computed tomography (MDCT) in screening for hepatocellular carcinoma (HCC) and to modify a liver CT protocol with a goal of dose reduction.	Computed tomography is primarily used to screen for HCC. Average estimated ED was 35.5 mSv. Unenhanced phase did not add to reader confidence; delayed phase increased confidence in 47% of cases. Thirty-two percent of the screening population had cumulative ED of greater than 200 mSv.	2
122. Van Thiel DH, Yong S, Li SD, Kennedy M, Brems J. The development of de novo hepatocellular carcinoma in patients on a liver transplant list: frequency, size, and assessment of current screening methods. Liver Transpl. 2004;10(5):631-637.	Observational-Dx	100 cases	To determine the frequency of new hepatic cancers since listing and evaluate the positive and negative predictive values of each assessment method over the surveillance interval.	The screening techniques utilized included quarterly alpha fetoprotein (alpha FP) determinations and ultrasound (US) studies as well as semi-annual triple phase computed tomography (CT) scans of the liver. alpha FP failed to identify any cases of de novo hepatic cancer in patients waiting for a liver transplant. In contrast, US and especially CT scanning with intravenous contrast identified new hepatic masses. The later method, which identified early enhancing mass lesions, was the more valuable method at identifying masses that subsequently were shown by pathologic examination of the explant liver to be hepatic cancers. However, only 14 of 20 individuals found to have a de novo tumor were identified by this method.	3
123. Valls C, Cos M, Figueras J, et al. Pretransplantation diagnosis and staging of hepatocellular carcinoma in patients with cirrhosis: value of dual-phase helical CT. AJR Am J Roentgenol. 2004;182(4):1011-1017.	Observational-Dx	85 patients	To prospectively evaluate the results of helical CT in the detection of hepatocellular carcinoma (HCC) in patients with cirrhosis undergoing orthotopic liver transplantation.	Pathologic examination found 85 cases of HCC in 51 patients. Helical CT enabled a correct diagnosis of HCC in 67 of 85 lesions for a sensitivity of 78.8%. HCC nodules were hypervascular in the arterial phase and hypovascular in the equilibrium phase in 63.5% (54/85) of patients. The false-negative rate was 21% (n = 18), and the positive predictive value was 88%. We had nine false-positive findings (11.8%) related to hemangiomas, transient hepatic attenuation differences, and regenerative nodules. Helical CT detected 61% (23/38) of lesions smaller than 2 cm and 93.6% (44/47) of lesions 2 cm or larger.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
124. Ronzoni A, Artioli D, Scardina R, et al. Role of MDCT in the diagnosis of hepatocellular carcinoma in patients with cirrhosis undergoing orthotopic liver transplantation. <i>AJR Am J Roentgenol.</i> 2007;189(4):792-798.	Observational-Dx	88 patients. Note: Multi-phase CT performed.	To assess the diagnostic performance of MDCT in the detection of hepatocellular carcinoma in patients with cirrhosis undergoing orthotopic liver transplantation.	Histopathologic examination revealed 139 hepatocellular carcinomas in 48 of the 88 patients. MDCT correctly depicted 89 of 139 hepatocellular carcinomas (sensitivity, 64%) at the original examination and 102 at reevaluation (sensitivity, 73.3%). Patient-by-patient analysis showed a specificity of 75% in the original reports and of 77.5% at reevaluation. A large number of false-positive nodules were found, most (59.2%) of them being smaller than 1 cm in diameter.	3
125. Lim KS. Diffusion-weighted MRI of hepatocellular carcinoma in cirrhosis. <i>Clin Radiol.</i> 2014;69(1):1-10.	Review/Other-Dx	N/A	To describe the strengths and weaknesses of the use of DWI in the diagnosis, grading, staging, and assessment of treatment response of HCC in cirrhosis, in light of the available evidence, complemented with illustrative cases.	The high efficacy of DWI in diagnosing HCC in cirrhosis justifies its inclusion in routine MRI protocols for cirrhotic nodules. However, the role of DWI in histological grading, staging, and prediction of treatment response, needs further evaluation	4
126. Lencioni R, Mascalchi M, Caramella D, Bartolozzi C. Small hepatocellular carcinoma: differentiation from adenomatous hyperplasia with color Doppler US and dynamic Gd-DTPA-enhanced MR imaging. <i>Abdom Imaging.</i> 1996;21(1):41-48.	Observational-Dx	38 patients	To investigate the usefulness of color Doppler ultrasound (US) and dynamic Gd-DTPA-enhanced magnetic resonance (MR) imaging in the differentiation of small hepatocellular carcinoma (HCC) and adenomatous hyperplasia (AH).	Color signals with pulsatile or continuous Doppler spectrum were demonstrated in 19 of 28 HCCs (68%) but in none of the AHs. Although there was considerable overlap in signal intensity between HCC and AH on both unenhanced T1- and T2-weighted images, early enhancement on breath-hold T1-weighted images obtained 40 s after starting contrast administration was observed in 22 of 28 HCCs (79%) but in none of the AHs. In 26 of 28 HCCs (93%), pulsatile or continuous flow at color Doppler US, early enhancement at dynamic MR imaging, or both were observed.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
127. Libbrecht L, Bielen D, Verslype C, et al. Focal lesions in cirrhotic explant livers: pathological evaluation and accuracy of pretransplantation imaging examinations. <i>Liver Transpl.</i> 2002;8(9):749-761.	Observational-Dx	52 patients	To evaluate the accuracy of different imaging techniques performed during pretransplantation evaluation.	Within 6 months before transplantation, color Doppler ultrasonography (US), contrast-enhanced computed tomography (CT), and magnetic resonance (MR) imaging were performed in 94%, 33%, and 55% of patients, respectively. In 2% to 8% of patients, different types of benign focal lesions were present, and a considerable proportion was interpreted as (pre)malignant on imaging examination. US detected only the largest HCCs (patient sensitivity, 40%; specificity, 100%) and no DNs. On a per-patient basis, contrast-enhanced CT and MR imaging had poor sensitivity (20% and 27%, respectively) and good specificity (100% and 94%, respectively) for DNs. Patient sensitivity and specificity of both techniques for HCC were reasonable (50% for CT, 70% for MR imaging) and good (79% for CT, 82% for MR imaging), respectively. Neither technique was able to detect smaller (pre)malignant lesions. As a consequence, 10% of patients underwent transplantation, although they exceeded the tumor number limit.	2
128. Park MJ, Kim YK, Lee MW, et al. Small hepatocellular carcinomas: improved sensitivity by combining gadoxetic acid-enhanced and diffusion-weighted MR imaging patterns. <i>Radiology.</i> 2012;264(3):761-770.	Observational-Dx	130 patients with confirmed small HCCs ($\leq 2.0\text{ cm}$) and 130 patients with cirrhosis without HCC	To determine if the combination of gadoxetic acid-enhanced magnetic resonance (MR) imaging and diffusion-weighted (DW) imaging helps to increase accuracy and sensitivity in the diagnosis of small hepatocellular carcinomas (HCCs) compared with those achieved by using each MR imaging technique alone.	The mean A(z) values for the combined set (0.952) were significantly higher than those for the gadoxetic acid set (A(z) = 0.902) or the DW imaging set alone (A(z) = 0.871) (P $\leq .008$). On a per-lesion basis, observers showed higher sensitivity in their analyses of the combined set (range, 91.1%-93.3% [163-167 of 179]) than in those of the gadoxetic acid set (range, 80.5%-82.1% [144-147 of 179]) or the DW imaging set alone (range, 77.7%-79.9% [139-143 of 179]) (P $\leq .003$). Positive predictive values and specificity for all observers were equivalent for the three imaging sets.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
129. Le Moigne F, Durieux M, Bancel B, et al. Impact of diffusion-weighted MR imaging on the characterization of small hepatocellular carcinoma in the cirrhotic liver. <i>Magn Reson Imaging</i> . 2012;30(5):656-665.	Observational-Dx	62 patients	To determine whether or not adding diffusion-weighted magnetic resonance imaging (DWI) to conventional magnetic resonance (MR) imaging sequences improves the characterization of small hepatocellular carcinoma (HCC) ($\leq 2\text{ cm}$) in the setting of cirrhotic liver compared to conventional sequences alone.	The area under the receiver operating characteristic curve for the second interpretation session (0.86) was significantly higher ($P=.038$) than that of the first session (0.76). The sensitivity was significantly increased from 75.7% to 87.8% by adding DWI to the conventional sequences ($P=.015$). No significant differences were observed for specificity values.	2
130. Kim YK, Lee WJ, Park MJ, Kim SH, Rhim H, Choi D. Hypovascular hypointense nodules on hepatobiliary phase gadoxetic acid-enhanced MR images in patients with cirrhosis: potential of DW imaging in predicting progression to hypervascular HCC. <i>Radiology</i> . 2012;265(1):104-114.	Observational-Dx	135 patients with hepatitis B-induced liver cirrhosis and 214 hypovascular hypointense nodules	To investigate the imaging features of hypovascular hypointense nodules on hepatobiliary phase gadoxetic acid-enhanced magnetic resonance (MR) images in patients with cirrhosis that may be associated with progression to hypervascular hepatocellular carcinoma (HCC).	On follow-up MR images, 139 nodules (65.0%) had no evidence of HCC (mean follow-up, 522 days) (group 1), but 75 (35.0%) became hypervascular HCC (mean follow-up, 388 days) (group 2). Univariable Cox analysis revealed that the degree of hypointensity on hepatobiliary phase images ($P=.044$ and $.001$) and hyperintensity on T2-weighted and DW images ($P=.001$ and $.0001$) was significantly related to the development of hypervascular HCC. According to the multivariable Cox analysis, no other variable significantly adjusted the model once hyperintensity at initial DW imaging was already included as an associated variable, (hazard ratio, 7.44; 95% confidence interval: 4.28, 12.94; $P=.0001$).	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
131. Hyodo T, Murakami T, Imai Y, et al. Hypovascular nodules in patients with chronic liver disease: risk factors for development of hypervascular hepatocellular carcinoma. <i>Radiology</i> . 2013;266(2):480-490.	Observational-Dx	68 patients	To identify patient characteristics and magnetic resonance (MR) imaging findings associated with subsequent hypervascularization in hypovascular nodules that show hypointensity on hepatobiliary phase gadoteric acid-enhanced MR images in patients with chronic liver diseases.	The prevalence of subsequent hypervascularization was 31% (50 of 160 nodules). Independent Cox multivariable predictors of increased risk of hypervascularization were hyperintensity on T2-weighted images (hazard ratio [HR] = 8.7; 95% confidence interval [CI]: 3.6, 20.8), previous local therapy for hypervascular HCC (HR = 5.0; 95% CI: 1.8, 13.6), Child-Pugh B cirrhosis (HR = 3.6; 95% CI: 1.4, 9.5) and coexistence of hypervascular HCC (HR = 2.0; 95% CI: 1.0, 3.8). The mean growth rate was significantly higher in nodules that showed subsequent hypervascularization than in those without hypervascularization. Kaplan-Meier analysis based on the receiver operating characteristic cutoff level (1.8×10^{-3} /day [tumor volume doubling time, 542 days]) showed that nodules with a higher growth rate had a significantly higher incidence of hypervascularization ($P = 5.2 \times 10^{-8}$, log-rank test).	3
132. Bartolozzi C, Battaglia V, Bargellini I, et al. Contrast-enhanced magnetic resonance imaging of 102 nodules in cirrhosis: correlation with histological findings on explanted livers. <i>Abdom Imaging</i> . 2013;38(2):290-296.	Observational-Dx	34 patients	To analyze Gd-EOB-DTPA-enhanced magnetic resonance (MR) findings of nodules (low-grade dysplastic nodules-LGDNs; high-grade dysplastic nodules-HGDN, and hepatocellular carcinoma-HCC), histologically identified on cirrhotic, explanted livers.	No differences were appreciable among ERs of HGDN and HCCs on HB phase ($P > 0.001$). Lesions' enhancement on vascular dynamic and on HB phases significantly correlated to histological classification of nodules ($P < 0.0001$). Nodular hyperintensity on arterial phase and hypointensity on late phase were highly predictive for HCC (PPV 100%), with a moderate sensitivity (72.5%). Nodular hypointensity on HB phase was detected on 39/40 HCCs (sensitivity 97.5%) and in 21/30 HGDNs, whereas no LGDN showed it.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
133. Gatto A, De Gaetano AM, Giuga M, et al. Differentiating hepatocellular carcinoma from dysplastic nodules at gadobenate dimeglumine-enhanced hepatobiliary-phase magnetic resonance imaging. <i>Abdom Imaging</i> . 2013;38(4):736-744.	Observational-Dx	25 patients	To evaluate whether the addition of delayed phase imaging (DPI) gadobenate dimeglumine-enhanced MRI to dynamic postcontrast imaging improves the characterization of small hepatocellular carcinoma (HCC) and the differentiation between HCC, high grade dysplastic nodules (HGDN), and low grade dysplastic nodules (LGDN).	All HCCs were hypointense on DPI while only 8 (57.1%) of 14 DN were hypointense and only 1 of 6 (16.6%) LGDNs was hypointense. There was a statistically significant difference in the hypointensity on DPI between HCCs and DNs ($p = 0.003$) in the qualitative analysis but not in the CNR values while there was a strong statistically significant difference in the hypointensity on DPI in the qualitative ($p = 0.00001$) and quantitative analysis ($p < 0.05$) between LGDNs and the group obtained by unifying HGDNs and HCCs.	3
134. Golfieri R, Grazioli L, Orlando E, et al. Which is the best MRI marker of malignancy for atypical cirrhotic nodules: hypointensity in hepatobiliary phase alone or combined with other features? Classification after Gd-EOB-DTPA administration. <i>J Magn Reson Imaging</i> . 2012;36(3):648-657.	Observational-Dx	111 atypical nodules detected in 77 consecutive Gd-EOB-DTPA-MRIs	To investigate whether the malignancy of atypical nodules in cirrhosis can be identified at gadoxetic-acid-disodium(Gd-EOB-DTPA)-MRI by their hypointensity in the hepatobiliary(HB)-phase alone or combined with any other MR imaging features.	Histology detected 60 benign and 51 malignant/premalignant nodules [10 overt hepatocellular carcinomas (HCCs) and 41 high-grade dysplastic nodules (HGDN)/early HCC]. Class IA contained 31 (94%) malignancies, IB one (3%), and IC only benign lesions. Class IIA had 100% malignancies, IIB three (37.5%) and IIC only two (28.5%). HB-phase hypointensity alone (Classes I-IIA) had 88% sensitivity, 91% NPV, and 93% diagnostic accuracy, superior ($P < 0.05$, $P < 0.006$, and $P < 0.05$, respectively) to any other MR imaging feature alone or combined	3
135. Ahn SS, Kim MJ, Lim JS, Hong HS, Chung YE, Choi JY. Added value of gadoxetic acid-enhanced hepatobiliary phase MR imaging in the diagnosis of hepatocellular carcinoma. <i>Radiology</i> . 2010;255(2):459-466.	Observational-Dx	59 patients	To determine the added value of hepatobiliary phase images in gadoxetic acid-enhanced magnetic resonance (MR) imaging in the evaluation of hepatocellular carcinoma (HCC).	For all observers, A z values were higher with the addition of the hepatobiliary phase. The observer who had the least experience in abdominal imaging (2 years) demonstrated significant improvement in A z , from 0.895 in set 1 to 0.951 in set 2 ($P = .049$). Sensitivity increased with the addition of hepatobiliary phase images but did not reach statistical significance. Nine HCCs (10.7%) in six patients (10.1%) were seen only on hepatobiliary phase images.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
136. Di Martino M, De Filippis G, De Santis A, et al. Hepatocellular carcinoma in cirrhotic patients: prospective comparison of US, CT and MR imaging. <i>Eur Radiol.</i> 2013;23(4):887-896.	Observational-Dx	140 patients	To prospectively compare the diagnostic performance of ultrasound (US), multidetector computed tomography (MDCT) and contrast-enhanced magnetic resonance imaging (MRI) in cirrhotic patients who were candidates for liver transplantation.	Significantly higher diagnostic accuracy, sensitivity and NPV was achieved on dynamic + hepatobiliary phase MRI compared with US, MDCT and dynamic phase MRI alone. The specificity and PPV of US was significantly lower than that of MDCT, dynamic phase MRI and dynamic + hepatobiliary phase MRI. Similar results were obtained for all sub-group analyses, with particular benefit for the diagnosis of smaller lesions between 1 and 2 cm.	2
137. Onishi H, Kim T, Imai Y, et al. Hypervascular hepatocellular carcinomas: detection with gadoxetate disodium-enhanced MR imaging and multiphasic multidetector CT. <i>Eur Radiol.</i> 2012;22(4):845-854.	Observational-Dx	31 patients	To retrospectively compare the accuracy of detection of hypervascular hepatocellular carcinoma (HCC) by multiphasic multidetector CT and by gadoxetate disodium-enhanced MR imaging.	The mean Az value for dynamic and hepatobiliary phase MR combined (0.81) or dynamic MR images alone (0.78) was significantly higher than that for CT images (0.67, $P < 0.001$, 0.005, respectively). The mean sensitivity of the combined MR images (0.67) was significantly higher than that of dynamic MR alone (0.52, $P < 0.05$) or CT images (0.44, $P < 0.05$). The mean positive predictive values were 0.96, 0.95 and 0.94, for CT, dynamic MR alone and combined MR images, respectively.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
138. Liu X, Zou L, Liu F, Zhou Y, Song B. Gadoteric acid disodium-enhanced magnetic resonance imaging for the detection of hepatocellular carcinoma: a meta-analysis. PLoS One. 2013;8(8):e70896.	Meta-analysis	10 citations	To determine the accuracy of MR imaging with gadoteric acid disodium (Gd-EOB-DTPA) for the detection of hepatocellular carcinoma (HCC).	: From 601 citations, 10 were included in the meta-analysis. The methodological quality of the 10 studies was good. Overall HCC: There was significant heterogeneity in the pooled analysis ($I^2 = 69.4\%$, $P = 0.0005$), and the pooled weighted values were determined to be sensitivity: 0.91 (95% confidence interval (CI): 0.89, 0.93); specificity: 0.95 (95% CI: 0.94, 0.96); diagnostic odds ratio: 169.94 (95% CI: 108.84, 265.36); positive likelihood ratio: 15.75 (95% CI: 7.45, 33.31); negative likelihood ratio: 0.10 (95% CI: 0.06, 0.15). The AUC was 0.9778. HCC in cirrhosis: The estimates were to be sensitivity: 0.91 (95% CI: 0.88, 0.93); specificity: 0.93 (95% CI: 0.89, 0.95); diagnostic odds ratio: 234.24 (95% CI: 33.47, 1639.25); positive likelihood ratio: 15.08 (95% CI: 2.20, 103.40); negative likelihood ratio: 0.08 (95% CI: 0.03, 0.21). The AUC was 0.9814. ≤ 20 mm HCC: The AUC was 0.9936. There was no notable publication bias.	M
139. Wu LM, Xu JR, Gu HY, et al. Is liver-specific gadoteric acid-enhanced magnetic resonance imaging a reliable tool for detection of hepatocellular carcinoma in patients with chronic liver disease? Dig Dis Sci. 2013;58(11):3313-3325.	Meta-analysis	10 studies of 570 patients	To perform a meta-analysis of all available studies of the diagnostic performance of gadoteric acid-enhanced MRI (Gd-EOB-MRI) for detection of HCC in patients with chronic liver disease.	Across 10 studies of 570 patients, Gd-EOB-MRI sensitivity was 0.91 (95% CI 0.77, 0.97) and specificity was 0.93 (95% CI 0.85, 0.97). Overall, LR+ was 13.6 (95% CI 5.6, 33.2), LR- was 0.10 (95% CI 0.04, 0.27), and DOR was 140.36 (95% CI 28, 696). Among patients with high pre-test probabilities, MRI enabled confirmation of HCC; among patients with low pre-test probabilities, MRI enabled exclusion of HCC. Worst-case-scenario (pre-test probability, 50%) post-test probabilities were 93 and 9% for positive and negative MRI results, respectively. In studies in which both Gd-EOB-MRI and contrast enhanced computed tomography (CE-CT) were performed, Gd-EOB-MRI was more sensitive than CE-CT (0.93 vs. 0.78; $p < 0.05$). Subgroup analysis suggested average lesion size (< 2 vs. > 2 cm) did not affect the diagnostic accuracy of the test ($p > 0.05$).	M

* See Last Page for Key

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
140. Kumada T, Toyoda H, Tada T, et al. Evolution of hypointense hepatocellular nodules observed only in the hepatobiliary phase of gadoxetate disodium-enhanced MRI. <i>AJR Am J Roentgenol.</i> 2011;197(1):58-63.	Observational-Dx	30 patients	To determine whether hypointense hepatocellular nodules observed in the hepatobiliary phase of MRI enhanced with gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid (gadoxetate disodium) progress to hypervascular hepatocellular carcinoma.	The overall 6- and 12-month cumulative incidences of vascularization were 27.6% and 43.5%. The 6- and 12-month cumulative incidences of vascularized nodules with a maximum diameter 15 mm or greater were 43.3% and 77.3% and a maximum diameter less than 15 mm were 16.9% and 16.9%. The difference between these incidences was significant (p = 0.0147).	3
141. Higaki A, Ito K, Tamada T, et al. High-risk nodules detected in the hepatobiliary phase of Gd-EOB-DTPA-enhanced MR imaging in cirrhosis or chronic hepatitis: incidence and predictive factors for hypervascular transformation, preliminary results. <i>J Magn Reson Imaging.</i> 2013;37(6):1377-1383.	Observational-Dx	43 patients	To evaluate the incidence and predictive factors of hypervascular transformation during follow-up of "high-risk nodules" detected in the hepatobiliary phase of initial Gd-EOB-DTPA-enhanced MRI in chronic liver disease patients.	The median observation period was 242.5 +/- 203.2 days (range, 47-802 days). Overall, 24 of 76 high-risk nodules (31.6%) showed hypervascular transformation during follow-up (median observation period, 186.0 +/- 190.3 days). The growth rate of the nodules (P < 0.001), the presence of fat within nodules (P = 0.037), and hyperintensity on T1-weighted images (P = 0.018) were significantly correlated with hypervascularization.	3
142. Tamada T, Ito K, Higaki A, et al. Gd-EOB-DTPA-enhanced MR imaging: evaluation of hepatic enhancement effects in normal and cirrhotic livers. <i>Eur J Radiol.</i> 2011;80(3):e311-316.	Observational-Dx	58 cirrhotic patients and 41 subjects with normal liver.	To assess differences in enhancement effects of liver parenchyma between normal and cirrhotic livers on contrast-enhanced MR imaging (CE-MRI) obtained with Gd-EOB-DTPA.	In normal-liver and Child-Pugh class A and B patients, mean RE of liver parenchyma increased significantly (P<0.03-0.001) with time until 20-min HP. Conversely, mean RE for Child-Pugh class C patients did not show any increasing tendency after PP. Mean RE of liver parenchyma at EP and HP (10-, 15- and 20-min) was highest in normal liver, followed by Child-Pugh class A, B and C cirrhosis (P<0.02-0.001).	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
143. Kim HY, Choi JY, Park CH, et al. Clinical factors predictive of insufficient liver enhancement on the hepatocyte-phase of Gd-EOB-DTPA-enhanced magnetic resonance imaging in patients with liver cirrhosis. <i>J Gastroenterol.</i> 2013;48(10):1180-1187.	Observational-Dx	328 patients	To clarify the factors predictive of liver enhancement in a relatively large sample of patients.	RE of patients with Child-Pugh A cirrhosis was significantly higher than that of patients with Child-Pugh B or C cirrhosis (both $P < 0.001$). Among various clinical factors, platelet count, prothrombin activity, albumin, sodium, total bilirubin, aspartate aminotransferase, Model for End-stage Liver Disease (MELD) score, MELD-Na score, Child-Pugh score, and the presence of ascites were significantly correlated with RE. A multiple stepwise regression analysis revealed that MELD-Na, albumin, and the presence of ascites were the only factors that predicted liver parenchymal enhancement on hepatocyte-phase images.	3
144. Verloh N, Haimerl M, Rennert J, et al. Impact of liver cirrhosis on liver enhancement at Gd-EOB-DTPA enhanced MRI at 3 Tesla. <i>Eur J Radiol.</i> 2013;82(10):1710-1715.	Observational-Dx	93 patients	To assess differences in enhancement effects of liver parenchyma between normal and cirrhotic livers on dynamic, Gd-EOB-DTPA enhanced MRI at 3T.	Mean RE was significantly different among all evaluated groups in the hepatobiliary phase and with increasing severity of liver cirrhosis, a decreasing, but still significant reduction of RE could be shown. Phase depending changes of RE for each group were observed. In case of non-cirrhotic liver or Child-Pugh Score A cirrhosis mean RE showed a significant increase between AP, LAP, PVP and HBP. For Child-Pugh B+C cirrhosis RE increased until PVP, however, there was no change in case of B cirrhosis ($p=0.501$) and significantly reduced in case of C cirrhosis ($p=0.043$) during HBP.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
145. Xu J, Igarashi S, Sasaki M, et al. Intrahepatic cholangiocarcinomas in cirrhosis are hypervascular in comparison with those in normal livers. Liver Int. 2012;32(7):1156-1164.	Review/Other-Dx	173 cases.	To compare the tumour vasculature.	It was found that ICC-cirrhosis and the cholangiocarcinoma component of HCC-ICC showed a higher density of arteries and microvessels (1.59 +/- 0.58/mm(2) (mean +/- SD) and 140 +/- 43/mm(2) in ICC-cirrhosis and 1.74 +/- 0.67/mm(2) and 131 +/- 46/mm(2) in the cholangiocarcinoma component of HCC-ICC than in ICC-reactive (1.26 +/- 0.61/mm(2) and 103 +/- 45/mm(2)). Dynamic computed tomography (CT) and magnetic resonance imaging (MRI) showed that a majority of ICC-cirrhosis displayed strong hypervascular enhancement, whereas one-third of ICC-reactive each showed strong, weak and no or minimal enhancement respectively. The increased vascular density was positively correlated with enhanced arterial phase of dynamic CT and MRI.	4
146. Anaparthi R, Talwalkar JA, Yin M, Roberts LR, Fidler JL, Ehman RL. Liver stiffness measurement by magnetic resonance elastography is not associated with developing hepatocellular carcinoma in subjects with compensated cirrhosis. Aliment Pharmacol Ther. 2011;34(1):83-91.	Observational-Dx	30 patients	To determine if liver stiffness of nonmalignant hepatic parenchyma using magnetic resonance elastography (MRE) is higher in patients with HCC compared with controls.	Thirty patients with HCC and 60 matched controls comprised the study cohort. The mean age for cases was 64+/-10 years (range, 45-85) with 70% being men. Major disease aetiologies were chronic viral hepatitis (57%), non-alcoholic fatty liver disease (33%) and alcohol (10%). Twenty-eight (93%) patients had solitary HCC lesions with a mean size of 5.2 cm (range, 2-14 cm). However, patients with HCC had similar liver stiffness among uninvolved areas distant to HCC lesions, when compared with controls without HCC (mean, 6.1+/-2.0 vs. 6.3+/-2.5 kPa, P=0.7).	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
147. Singh S, Fujii LL, Murad MH, et al. Liver stiffness is associated with risk of decompensation, liver cancer, and death in patients with chronic liver diseases: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2013;11(12):1573-1584 e1571-1572; quiz e1588-1579.	Meta-analysis	17 studies, reporting on 7058 patients	To evaluate the association between LSM and outcomes of patients with CLDs.	Our final analysis included 17 studies, reporting on 7058 patients with CLDs. Baseline LSM was associated significantly with risk of hepatic decompensation (6 studies; RR, 1.07; 95% CI, 1.03-1.11), HCC (9 studies; RR, 1.11; 95% CI, 1.05-1.18), death (5 studies; RR, 1.22; 95% CI, 1.05-1.43), or a composite of these outcomes (7 studies; RR, 1.32; 95% CI, 1.16-1.51). We observed considerable heterogeneity among studies-primarily in the magnitude of effect, rather than the direction of effect. This heterogeneity could not be explained by variations in study locations, etiologies and stages of CLD, techniques to measure liver stiffness, adjustment for covariates, or method of imputing relationship in the meta-analysis.	M
148. Delbeke D, Martin WH, Sandler MP, Chapman WC, Wright JK, Jr., Pinson CW. Evaluation of benign vs malignant hepatic lesions with positron emission tomography. Arch Surg. 1998;133(5):510-515; discussion 515-516.	Observational-Dx	110 consecutive patients	To assess the value of FDG-PET to differentiate benign from malignant hepatic lesions and to determine in which types of hepatic tumors PET can help evaluate stage, monitor response to therapy, and detect recurrence in prospective blinded-comparison clinical cohort study.	All (100%) liver metastases from adenocarcinoma and sarcoma primaries in 66 patients and all cholangiocarcinomas in 8 patients had increased uptake values, liver background ratios greater than 2, and an SUV greater than 3.5. Hepatocellular carcinoma had increased FDG uptake in 16/23 patients and poor uptake in 7 patients. All benign hepatic lesions (n=23), including adenoma and fibronodular hyperplasia, had poor uptake, an liver background ratio of less than 2, and an SUV less than 3.5, except for 1/3 abscesses that had definite uptake. The PET technique using FDG static imaging was useful to differentiate malignant from benign lesions in the liver. Limitations include false-positive results in a minority of abscesses and false-negative results in a minority of hepatocellular carcinoma. The PET technique was useful in tumor staging and detection of recurrence, as well as monitoring response to therapy for all adenocarcinomas and sarcomas and most hepatocellular carcinomas. Therefore, pretherapy PET imaging is recommended to help assess new hepatic lesions.	3

* See Last Page for Key

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
149. Khan MA, Combs CS, Brunt EM, et al. Positron emission tomography scanning in the evaluation of hepatocellular carcinoma. J Hepatol. 2000;32(5):792-797.	Observational-Dx	20 patients	To evaluate the role of PET imaging in the diagnosis of hepatocellular carcinoma.	Of the 20 patients studied, 11 (55%) had positive PET scans (PET score: 3 or 4) while nine (45%) were negative (PET score: 1 or 2). CT scan was positive in 18 patients (90%) and negative in two (10%). PET, however, revealed metastases in three patients that were not seen on CT. On pathological review, well-differentiated and low-grade tumors had lower PET scores. Comparison of the well-differentiated with the moderately- and poorly-differentiated tumors revealed a statistically significant difference. No statistical significance was observed between the moderately- and poorly-differentiated tumors or between different tumor grades and PET scores	3
150. Trojan J, Schroeder O, Raedle J, et al. Fluorine-18 FDG positron emission tomography for imaging of hepatocellular carcinoma. Am J Gastroenterol. 1999;94(11):3314-3319.	Observational-Dx	14 patients	To evaluate the sensitivity of 18F-FDG PET for the imaging and staging of histologically confirmed HCC.	In 7 patients PET demonstrated increased tumor 18F-FDG uptake, whereas HCC was not distinguishable from nonmalignant liver tissue in 7 other patients. Hepatic lesions were detected by ultrasonography in all patients, whereas only 11 of 14 HCCs could be identified by CT. In 3 patients extrahepatic spread was demonstrated by 18F-FDG PET. Patients with increased tumor 18F-FDG uptake had significantly larger hepatic lesions and higher serum AFP levels than those with normal 18F-FDG uptake. Lesions could be visualized by 18F-FDG PET in 7 of 8 patients with moderately or poorly differentiated HCC, whereas none of the six well-differentiated tumors was detected. Two patients with strong p53 expression demonstrated increased tumor 18F-FDG uptake and extrahepatic metastases	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
151. Kim BK, Kang WJ, Kim JK, et al. 18F-fluorodeoxyglucose uptake on positron emission tomography as a prognostic predictor in locally advanced hepatocellular carcinoma. <i>Cancer</i> . 2011;117(20):4779-4787.	Observational-Dx	107 patients	To investigate the value of metabolic activity assessed by 18F-FDG-PET as a prognostic factor in patients who were treated with localized CCRT followed by HAIC for locally advanced HCCs.	The median maximal tumor SUV was 6.1 (range, 2.4- approximately 19.2). Patients with low maximal tumor SUVs (<6.1) had a higher disease control rate than those with high maximal tumor SUVs (≥ 6.1) (86.8% vs 68.5%, respectively, $P = .023$). Both median progression-free survival (PFS; 8.4 vs 5.2 months; $P = .003$) and overall survival (OS; 17.9 vs 11.3 months; $P = .013$) were significantly longer in the low maximal tumor SUV group than in the high maximal tumor SUV group, respectively. In multivariate analysis, low maximal tumor SUV and objective responses to CCRT remained significant for PFS and OS. The high maximal tumor SUV group was more likely to have extrahepatic metastasis within 6 months than the low maximal tumor SUV group (58.1% vs 26.8%, respectively; $P < .001$). Similar results were obtained for the maximal tumor SUV/normal liver maximal SUV ratio (< 2 vs ≥ 2) concerning progression, death, and extrahepatic metastasis.	2
152. Castilla-Lievre MA, Franco D, Gervais P, et al. Diagnostic value of combining (11)C-choline and (18)F-FDG PET/CT in hepatocellular carcinoma. <i>Eur J Nucl Med Mol Imaging</i> . 2016;43(5):852-859.	Observational-Dx	33 patients	To emphasize the diagnostic value of combining (11)C-choline and (18)F-FDG PET/CT for hepatocellular carcinoma (HCC) in patients with chronic liver disease.	Twenty-eight HCC, four cholangiocarcinomas and one adenoma were diagnosed. In the HCC patients, the sensitivity of (11)C-choline, (18)F-FDG and combined (11)C-choline and (18)F-FDG PET/CT for the detection of HCC was 75 %, 36 % and 93 %, respectively. Serum alpha-fetoprotein levels > 200 ng/ml were more frequent among patients with (18)F-FDG-positive lesions than those with (18)F-FDG-negative lesions ($p < 0.05$). Early recurrence ($n=2$) or early death ($n=5$) occurred more frequently in patients with (18)F-FDG-positive lesions than in those with (18)F-FDG-negative lesions ($p < 0.05$).	2
153. American College of Radiology. ACR Appropriateness Criteria®: Radiologic Management of Hepatic Malignancy. Available at: https://acsearch.acr.org/docs/69379/Narrative/ .	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for a specific clinical condition.	No results stated in abstract.	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
154. Gaba RC. Chemoembolization practice patterns and technical methods among interventional radiologists: results of an online survey. AJR Am J Roentgenol. 2012;198(3):692-699.	Observational-Dx	268 respondents	To assess patterns of chemoembolization use; identify variations in application, technique, and follow-up; and recognize areas of practice conformity and divergence.	Two hundred sixty-eight of 1157 invited SIR members (23%) answered the 34-item survey. Respondents were predominantly male (93%) fellowship-trained full-time interventional radiologists (IRs) (87%) in practice for less than 15 years (69%) at community hospitals (61%) in the United States (91%). IRs (53%) most commonly drove therapeutic decision making. Most respondents (61%) performed 1-5 chemoembolizations per month and preferred drug-eluting beads to iodized oil for unifocal (46% vs 39%, respectively) and multifocal (40% vs 30%) hepatocellular carcinoma (HCC), although (90%)Y radioembolization was favored when portal vein thrombosis was present (48% vs 28%). IRs showed variability in recognized procedure contraindications. Most respondents agreed on chemotherapeutic regimen but showed variable particle embolization use (17-45%) during oily chemoembolization. The 100- to 300-mum (49%) LC Beads (AngioDynamics) (65%) were the favored drug-eluting beads. Lobar chemoembolization was preferred. Treatment endpoints lacked consensus, but substasis was most desirable (56%). Up to 19% of respondents performed outpatient chemoembolization. Concurrent percutaneous ablation was infrequently used (applied in 0-25% of cases by 61-91% of respondents). Most (up to 74%) IRs preferred CT follow-up with the decision for retreatment based on CT evidence of viable disease (93%).	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
155. Gaba RC, Baerlocher MO, Nikolic B, Venkatesan AM, Lewandowski RJ. Clinical and Imaging Follow-up Practices after Transarterial Therapy for Primary and Secondary Hepatic Malignancies: Results of an Online Survey. <i>Acad Radiol.</i> 2015;22(12):1510-1515.	Review/Other-Dx	361 respondents	To characterize practices and quantify variation in longitudinal follow-up approaches among interventional radiologists (IRs) after liver transarterial locoregional therapy (LRT) in contemporary Interventional Oncology practice.	The 30-item survey response rate was 11% (361 of 3290). Respondents were predominantly American IRs (311 of 355, 88%) who perform 1-5 LRTs monthly (196 of 354, 55%). Most (305 of 336, 91%) IRs reported longitudinal follow-up, with patient encounters within 1-month (73%, 211 of 290) postprocedure and every 3 months (68%, 196 of 287) thereafter and involvement in imaging (up to 80%, 235 of 290) ordering and evaluation. Preferred timing of first follow-up imaging (1 month vs. 3 months) and response criteria used (mRECIST favored) varied. CONCLUSIONS: Although IRs are actively involved in clinical and imaging follow-up of patients with liver malignancies treated with transarterial LRTs, there are differences	4
156. NCCN Clinical Practice Guidelines in Oncology. Hepatobiliary Cancers. Version 2.2016. 2016; Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf .	Review/Other-Dx	N/A	To provide recommendations regarding the management of patients with hepatobiliary cancers.	No results stated in abstract.	4
157. Boas FE, Do B, Louie JD, et al. Optimal imaging surveillance schedules after liver-directed therapy for hepatocellular carcinoma. <i>J Vasc Interv Radiol.</i> 2015;26(1):69-73.	Review/Other-Dx	910 patients	To optimize surveillance schedules for the detection of recurrent hepatocellular carcinoma (HCC) after liver-directed therapy.	Recurrence is 6.5 times more likely in the first year after treatment than in the second. Therefore, screening should be much more frequent in the first year. For eight time points in the first 2 years of follow-up, the optimal schedule is 2, 4, 6, 8, 11, 14, 18, and 24 months. This schedule reduces diagnostic delay compared with published schedules and is cost-effective.	4
158. Chiu RY, Yap WW, Patel R, Liu D, Klass D, Harris AC. Hepatocellular Carcinoma Post Embolotherapy: Imaging Appearances and Pitfalls on Computed Tomography and Magnetic Resonance Imaging. <i>Can Assoc Radiol J.</i> 2016;67(2):158-172.	Review/Other-Dx	N/A	To discuss the imaging appearances and pitfalls of HCCs following embolotherapies on CT and MRI.	No results stated in abstract.	4

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
159. Okada M, Kim T, Murakami T. Hepatocellular nodules in liver cirrhosis: state of the art CT evaluation (perfusion CT/volume helical shuttle scan/dual-energy CT, etc.). <i>Abdom Imaging</i> . 2011;36(3):273-281.	Review/Other-Dx	N/A	To explain the role of advanced liver CT imaging, including perfusion CT, dual-energy CT, and volume helical shuttle (VHS) scanning, with regard to its clinical applications.	Perfusion CT is a promising method for calculating hepatic blood flow and portal blood flow, including microcirculation, using a color-encoded display of parameters obtained from the liver time-density curve, with iodine contrast agent. Tumor angiogenesis and assessment of the response to antiangiogenesis treatment (e.g., Sorafenib) can be analyzed by perfusion CT of the liver. VHS scan has very high temporal resolution due to the reciprocating movement employed during scanning, enabling the acquisition of 24 scans of the whole liver in the arterial dominant phase during a 40-s breath hold, and a reduction in radiation dose. Dual-energy CT enables differentiation of materials and tissues based on their CT density values, using two different energy spectra. This method includes a low tube voltage CT technique that increases the contrast enhancement of vascular structures while simultaneously reducing radiation dose. Images obtained at the preferred settings of low tube voltage and high tube current, with dose reduction in the hepatic arterial phase, are useful for detecting hypervascular hepatocellular carcinoma.	4
160. Yu JS, Kim YH, Rofsky NM. Dynamic subtraction magnetic resonance imaging of cirrhotic liver: assessment of high signal intensity lesions on nonenhanced T1-weighted images. <i>J Comput Assist Tomogr</i> . 2005;29(1):51-58.	Observational-Dx	104 hyperintense lesions	To determine the technical feasibility and value of dynamic subtraction (postcontrast-precontrast) magnetic resonance (MR) imaging for the assessment of hyperintense lesions on precontrast T1-weighted images in the cirrhotic liver.	The quality of subtraction images was always diagnostic for lesions larger than 2 cm in diameter (n=8) but not diagnostic for 73% (40 of 55 lesions) of small subcentimetric lesions. Thirty-one subcapsular lesions always showed a variable degree of coregistration artifact. Only 3 of 35 lesions with a slice misregistration of 3 mm or more gave rise to subtraction images of diagnostic quality. For determining the contrast enhancement, the area under the receiver operating characteristic curve of 30 verified lesions was significantly larger (P <0.001) for subtraction images than for conventional arterial phase images.	3

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
161. Liu LN, Xu HX, Zhang YF, Xu JM. Hepatocellular carcinoma after ablation: the imaging follow-up scheme. World J Gastroenterol. 2013;19(6):797-801.	Review/Other-Dx	N/A	To discuss the discordance between CT and CEUS, as well as the underlying mechanisms involved.	No results stated in abstract.	4
162. Roccarina D, Garcovich M, Ainora ME, et al. Usefulness of contrast enhanced ultrasound in monitoring therapeutic response after hepatocellular carcinoma treatment. World J Hepatol. 2015;7(14):1866-1874.	Review/Other-Dx	N/A	To give an overview of the current status of CEUS in monitoring hepatocellular carcinoma response to different kind of treatments.	No results stated in abstract.	4
163. Zheng SG, Xu HX, Lu MD, et al. Role of contrast-enhanced ultrasound in follow-up assessment after ablation for hepatocellular carcinoma. World J Gastroenterol. 2013;19(6):855-865.	Observational-Dx	141	To assess the usefulness of contrast-enhanced ultrasound (CEUS) during follow-up after percutaneous ablation therapy for hepatocellular carcinoma (HCC).	During a follow-up period of 1-31 mo (median, 4 mo), 169 paired CEUS and CECT examinations were carried out for the 141 patients. For a total of 221 ablated lesions, 266 comparisons between CEUS and CECT findings were performed. Thirty-three LTPs were detected on CEUS whereas 40 LTPs were detected on CECT, there was significant difference ($P < 0.001$). In comparison with CECT, the numbers of false positive and false negative LTPs detected on CEUS were 6 and 13, respectively; the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy of CEUS in detecting LTPs were 67.5%, 97.4%, 81.8%, 94.4% and 92.3%, respectively. Meanwhile, 131 new intrahepatic recurrent foci were detected on CEUS whereas 183 were detected on CECT, there was also significant difference ($P < 0.05$). In comparison with CECT, the numbers of false positive and false negative intrahepatic recurrences detected on CEUS were 13 and 65, respectively; the sensitivity, specificity, PPV, NPV and overall accuracy of CEUS in detecting new intrahepatic recurrent foci were 77.7%, 92.0%, 92.4%, 76.7% and 84.0%, respectively.	2

**Chronic Liver Disease
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
164. Guibal A, Bertin C, Egels S, Savier E, Grenier PA, Lucidarme O. Contrast-enhanced ultrasound (CEUS) follow-up after radiofrequency ablation or cryoablation of focal liver lesions: treated-area patterns and their changes over time. Eur Radiol. 2013;23(5):1392-1400.	Observational-Dx	39 patients	To describe the early patterns of liver lesions successfully treated with radiofrequency ablation (RFA) or cryoablation (CA) and their changes over time.	After contrast enhancement, shortly after ablation, undefined margins with persistent enhancing small vessels penetrating >2 mm into the treated zone were significantly more frequent after CA (67 %) than RFA (22 %) (P < 0.02). During the arterial phase, a thin, enhancing marginal rim was seen during week 1 (T1) in around 28 % of RF lesions, while 75 % of cryolesions had thick enhancing rims (P < 0.02). The mean RF-induced lesion volume, maximum at T1 (44.1 +/- 37.5 ml), shrank slowly over time, remaining clearly visible at 1 year (8.3 +/- 7.4 ml). Cryolesions shrank faster (P = 0.009), from an average of 16.6 +/- 7.1 ml at T1 to 1.7 +/- 1.3 ml 1-year post-ablation.	2
165. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: http://www.acr.org/~media/ACR/Documents/AppCriteria/RadiationDoseAssessmentIntro.pdf .	Review/Other-Dx	N/A	Guidance document on exposure of patients to ionizing radiation.	N/A	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1:* The study is well-designed and accounts for common biases.
- *Category 2:* The study is moderately well-designed and accounts for most common biases.
- *Category 3:* There are important study design limitations.
- *Category 4:* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
 - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
 - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
 - c) the study is an expert opinion or consensus document.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment