Published in final edited form as:

J Comput Assist Tomogr. 2008 ; 32(2): 198–203. doi:10.1097/RCT.0b013e31815ea857.

Diagnosis of Cirrhosis by Spiral Computed Tomography: A Case-Control Study With Feature Analysis and Assessment of Interobserver Agreement

Alexander Keedy, BS, Antonio C. Westphalen, MD, Aliya Qayyum, MBBS, Rizwan Aslam, MBBS, Alexander V. Rybkin, MD, Mei-Hsiu Chen, PhD, and Fergus V. Coakley, MD, MB, BCh
From the Department of Radiology, University of California, San Francisco, San Francisco, CA

Abstract

Purpose—To determine the accuracy and interobserver agreement of spiral computed tomography (CT) in the diagnosis of cirrhosis.

Materials and Methods—We retrospectively identified 126 patients who underwent spiral CT at our institution and who had a contemporaneous histopathologic confirmation of cirrhosis ($n = 67$) or clinical and biochemical evidence of a normal liver ($n = 59$). Two experienced readers independently recorded the overall likelihood of cirrhosis and the presence or absence of hepatic and extrahepatic findings of cirrhosis and portal hypertension on a 5-point scale from 1 (definitely absent) to 5 (definitely present/severe).

Results—Receiver operating characteristic curve and κ statistic analyses showed that the overall likelihood of cirrhosis was the most accurate and objective observation, with an area under the curve (AUC) of 0.97 for reader 1 and 0.90 for reader 2 and a κ value of 0.70. Individual findings that were accurate and objective were diaphragmatic surface nodularity (AUC = 0.95 and 0.88 for readers 1 and 2, respectively, $\kappa = 0.75$), global or segmental volume loss (AUC = 0.95 and 0.87 for readers 1 and 2, respectively, $\kappa = 0.70$), and superior diaphragmatic adenopathy (AUC = 0.85 for both readers, $\kappa = 0.78$). Of note, portal vein diameter was not significantly different between normal and cirrhotic patients as measured by either reader ($P = 0.54$ and 0.65).

Conclusion—Spiral CT demonstrates high accuracy and interobserver agreement in the diagnosis of cirrhosis, suggesting CT may be a supplementary diagnostic test in patients who have contraindications to biopsy or have equivocal biopsy findings.

Keywords

cirrhosis; computed tomography

Cirrhosis is a process of irreversible hepatic nodular regeneration and fibrosis and is the nonspecific result of repeated episodes of hepatocellular injury from a variety of causes including chronic viral hepatitis and exposure to toxins such as alcohol. Liver biopsy is generally and traditionally regarded as the reference standard for the diagnosis of cirrhosis,¹ but may yield false-negative results in up to one third of cases^{2,3} and is an invasive procedure with a reported complication rate of 3.7%.^{1,4} Given the limitations of biopsy, it is unsurprising

that a range of biochemical and imaging markers have been investigated for the noninvasive evaluation of hepatic fibrosis and cirrhosis.^{5,6} What is surprising is that although there have been several detailed reports describing computed tomography (CT) findings in established cirrhosis,^{7–9} the role of CT in the diagnosis of cirrhosis has received little attention. In particular, the diagnostic accuracy and interobserver agreement of the reported morphological changes at CT in cirrhosis have not been reported. This is of practical importance because with the increasing use of CT, it is not uncommon to encounter a patient with hepatic surface nodularity as an unexpected finding. A referring clinician who receives a report of such a finding might reasonably ask the predictive value and interobserver agreement of the observation. Therefore, we undertook this study to determine the accuracy and interobserver agreement of spiral CT in the diagnosis of cirrhosis, using a case-control study with feature analysis.

MATERIALS AND METHODS

Patients

This was a retrospective single-institutional study that was approved by our institutional Committee on Human Research with waiver of the requirement for written consent. The study was compliant with the Health Insurance Portability and Accountability Act. We searched our radiology and pathology information systems to identify patients who met the following inclusion criteria:

1. contrast-enhanced CT of the abdomen performed between October 1997 and December 2002, and
2. contemporaneous histopathologic confirmation of cirrhosis (based on examination of liver tissue obtained either by biopsy or surgical resection) or confirmation of a normal liver (based on histopathologic findings or a combination of a lack of risk factors for hepatic disease, absence of any symptoms or signs of liver disease, and normal hepatic biochemistry).

One hundred twenty-six patients met these criteria and consisted of 67 patients with cirrhosis and 59 patients without cirrhosis. Additional clinical data were compiled by review of all available medical records. The cirrhotic group consisted of 39 men and 28 women with a mean age of 51 years (range, 19–78 years). The diagnosis of cirrhosis was established by histopathologic examination of specimens from liver transplantation ($n = 36$), needle biopsy ($n = 27$), or autopsy ($n = 4$). In 57 patients, CT was performed before the histopathologic examination with a mean elapsed time of 80 days (range, 0–778 days). In 10 patients, CT was performed after the histopathologic examination with a mean elapsed time of 224 days (range, 1–1053 days). The causes of cirrhosis were chronic viral hepatitis B and/or C ($n = 31$), cryptogenic cirrhosis ($n = 17$), primary sclerosing cholangitis ($n = 9$), primary biliary cirrhosis ($n = 5$), Budd-Chiari syndrome ($n = 2$), hepatitis C and ethanol abuse ($n = 1$), ethanol abuse ($n = 1$), and nonalcoholic steatohepatitis ($n = 1$). The severity of cirrhosis was assessed by the Child-Turcotte-Pugh classification,^{10,11} with 12 patients in class A, 15 in class B, 32 in class C, and 8 undeterminable. The noncirrhotic group consisted of 35 men and 24 women with a mean age of 42 years (range, 18–82 years). The diagnosis of a normal liver was established by biopsy in 11 patients. These patients had a normal liver histology, without fibrosis. Biopsy was performed as part of potential living related donor workup in 9 patients and for suspected hepatic malignancy in 2 cases. In these cases, CT was performed before the histopathologic examination with a mean elapsed time of 62 days (range, 5–254 days). The remaining 48 patients were judged clinically to not have cirrhosis based on a combination of a lack of risk factors for hepatic disease, absence of any symptoms or signs of liver disease, and normal hepatic biochemistry. The indications for abdominal CT in the noncirrhotic group were

assessment for potential liver donation (n = 41), cancer-related follow-up (n = 7), suspected gastrointestinal pathology (n = 6), abdominal pain (n = 3), or postsurgical follow-up (n = 2).

CT Technique

Computed tomographic examinations were performed on either 4-row (n = 79) or 16-row (n = 47) multidetector CT scanners (Light Speed or HiSpeed; General Electric Medical Systems, Milwaukee, Wis) after the power injection of 150 mL intravenous iohexol (Omnipaque 350; Nycomed Amersham, Princeton, NJ) at a rate of 2 to 5 mL/s. In the cirrhotic group and control group, 64 and 21 patients, respectively, also received 800 mL oral diatrizoate meglumine (Hypaque; Nycomed, Amersham). Additional details of CT technique are shown in Table 1.

CT Interpretation

Two attending radiologists specializing in abdominal imaging (A.C.W., F.V.C.) independently reviewed all the CT images on a picture archiving and communication system workstation (Impax; Agfa, Mortsels, Belgium). The cases were arranged in random order, and readers were unaware of all clinical and histopathologic findings. We selected a variety of CT findings related to cirrhosis and portal hypertension for feature analysis, based on review of the existing literature⁷⁻⁹ and the authors' experience. Accordingly, the following CT signs were ranked on a 5-point scale (1 = absent, 2 = equivocal/indeterminate, 3 = present and mild, 4 = present and moderate, and 5 = present and marked): diaphragmatic surface nodularity, visceral surface nodularity, global or segmental volume loss, caudate lobe hypertrophy, parenchymal heterogeneity, corkscrew vessels, rounded left liver lobe tip, small right liver lobe, varices, ascites, gall bladder wall thickening, small- or large-bowel wall thickening, and overall impression. The following measurements were recorded: short-axis diameter of the main portal vein measured midway between the splenorenal confluence and porta hepatis¹²; short-axis diameter of the largest periportal, retroperitoneal, and superior diaphragmatic lymph nodes; and the craniocaudal length of the spleen. The presence or absence of paraumbilical, splenorenal, gastroesophageal, or other portosystemic varices was also recorded.

Statistical Analysis

Statistical analysis was performed using MedCalc Software, version 7.4.3.0 (MedCalc Software, Mariakerke, Belgium). Area under the receiver operating characteristic curve (AUC) analysis was used to evaluate the diagnostic accuracy of individual CT signs of cirrhosis that were scored on a 5-point scale. The presence or absence of portosystemic varices was examined using the χ^2 test for proportions. All other data were examined using the 2-tailed *t* test. These tests were performed separately for each observer. Interobserver agreement was assessed with linearly weighted κ statistics for categorical variables and Pearson correlation coefficient for continuous variables. The level of agreement was defined as follows: κ = 0 to 0.20, poor agreement; κ = 0.21 to 0.40, fair agreement; κ = 0.41 to 0.60, moderate agreement; κ = 0.61 to 0.80, good agreement; and κ = 0.81 to 1.00, very good agreement.¹³

RESULTS

The results of the receiver operating characteristic curve analyses with respect to accuracy in the diagnosis of cirrhosis (AUC values) and interobserver agreement (κ values or Pearson correlation coefficients) are shown in Table 2 and Figure 1. Representative examples of a selection of specific CT signs are shown in Figure 2–Figure 6. The established findings of cirrhosis and portal hypertension were generally accurate in the distinction of cirrhotic and noncirrhotic patients, and the signs were generally objective (high interobserver agreement). Inspection of the results showed that the overall likelihood of cirrhosis, as judged by the readers, was the single most accurate and objective observation, with an AUC of 0.97 for reader 1 and 0.90 for reader 2 and a κ value of 0.70. Individual findings that were both accurate and objective

were diaphragmatic surface nodularity (AUC = 0.95 and 0.88 for readers 1 and 2, respectively, $\kappa = 0.75$), global or segmental volume loss (AUC = 0.95 and 0.87 for readers 1 and 2, respectively, $\kappa = 0.70$), and superior diaphragmatic adenopathy (AUC = 0.85 for both readers, $\kappa = 0.78$). Of note, portal vein diameter was not significantly different between normal and cirrhotic patients as measured by either reader ($P = 0.54$ and 0.65).

DISCUSSION

Radiologists are generally familiar with the hepatic and extrahepatic CT findings in cirrhosis and probably consider the diagnosis to be relatively straightforward, but the diagnostic accuracy and interobserver variability of these observations have been poorly explored. Our study indicates that CT has high accuracy and interobserver agreement in the diagnosis of cirrhosis. This conclusion could be of clinical importance in several settings. For example, given the increasing use of CT, it is not uncommon to see a nodular liver as an incidental finding, and our study now provides a basis for reporting this as strongly suggestive of cirrhosis. As another example, it is conceivable that imaging might supplement biopsy in a patient with chronic liver disease and a needle biopsy demonstrating fibrosis that not did reach the histopathologic threshold for cirrhosis; again, the finding of hepatic nodularity would point heavily toward a diagnosis of cirrhosis in such a scenario. With respect to the specific signs that we studied, it would seem that overall reader impression is the single most accurate and reproducible observation in the diagnosis of cirrhosis (AUC = 0.97 for reader 1 and 0.90 for reader 2, $\kappa = 0.70$). Diaphragmatic surface nodularity, global or segmental volume loss, and superior diaphragmatic adenopathy were also accurate and reproducible. The finding that diaphragmatic surface nodularity appeared to have higher interobserver agreement than visceral surface nodularity is interesting and may reflect a greater degree of subjectivity in the identification of nodularity on the undersurface of the liver, which is normally somewhat more irregular in contour due to the greater number of anatomic markings.

Our results add to prior research in imaging of cirrhosis. In this regard, an interesting finding in our study was the absence of any statistically significant difference in portal vein diameter between the cirrhotic and noncirrhotic groups. This contradicts the suggestion in sonography studies that an increased portal vein diameter is suggestive of portal hypertension,¹⁴ and, if anything, our result is more in keeping with a prior CT study showing that hepatofugal flow in cirrhosis is associated with a reduced portal vein diameter.¹² Undue significance may be currently placed on the measurement of portal vein diameter at sonography of the cirrhotic liver. In a prospective study, the presence or absence of anterior hepatic surface nodularity at high-resolution sonography (7.5 MHz) was assessed in 100 patients with suspected liver disease. All patients underwent biopsy or laparoscopy, and 49 were proven to have cirrhosis.¹⁵ An overall diagnostic accuracy of 88% was reported, relatively similar to our AUC values of 0.95 and 0.88 for readers 1 and 2 using diaphragmatic surface nodularity as a diagnostic sign of cirrhosis, but all studies appear to have been performed by a single reader, and no interobserver agreement was reported.

Our study has several limitations. Our control group consisted mainly of healthy potential liver donors and did not include any substantial number of patients with diseases that might produce CT findings mimicking cirrhosis or portal hypertension. Our subject group may also have been slightly skewed to those with more severe cirrhosis and possibly more marked CT signs, with 12 patients in Child-Turcotte-Pugh class A, 15 in class B, and 32 in class C (8 undeterminable). As such, our results may overestimate the accuracy and reproducibility of CT in the diagnosis of cirrhosis when applied to a more general population. For example, superior diaphragmatic adenopathy is common in cirrhotics¹⁶ but can also be seen in chronic hepatitis, ovarian cancer, and other conditions.^{17–19} Our control group was composed predominantly of healthy potential liver donors and did not include any patients with chronic hepatitis, so that the value of superior

diaphragmatic adenopathy in the distinction of cirrhotic and noncirrhotic patients is likely exaggerated. We scored CT signs of cirrhosis on what could arguably be described as a subjective and arbitrary 5-point scale; however, the high degree of interobserver agreement we documented between the 2 readers would suggest that the findings are relatively objective and reproducibly recorded by different radiologists. We have attempted to assess CT signs of cirrhosis based on a combination of accuracy and interobserver agreement (Table 2 and Fig. 1). Although high values for both parameters are clearly desirable, we are unaware of any statistical test that allows simultaneous comparison of both parameters to determine which CT signs are globally and significantly better; as such, the importance of our results is open to interpretation. Still, we believe that our study is of value in providing a preliminary overview of the accuracy and reproducibility of CT and individual CT findings in the diagnosis of cirrhosis. Finally, although we tried to study the individual CT signs of cirrhosis, it is inevitable that these will be heavily interdependent, because all are manifestations of a single diagnosis and because readers may be more likely to call a CT sign of cirrhosis as present when they have found other signs of cirrhosis. For example, such interdependence precluded performance of multivariate analysis on our data set.

In conclusion, spiral CT demonstrates high accuracy and interobserver agreement in the diagnosis of cirrhosis, suggesting CT may be a supplementary diagnostic test in patients who have contraindications to biopsy or have equivocal biopsy findings.

REFERENCES

1. Reddy SI, Grace ND. Liver imaging: a hepatologist's perspective. *Clin Liver Dis* 2002;6:297–310. [PubMed: 11933595]
2. Piccinino F, Sagnelli E, Pasquale G, et al. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. *J Hepatol* 1986;2:165–173. [PubMed: 3958472]
3. Ponichak J, Bernstein DE, Reddy KR, et al. The role of laparoscopy in the diagnosis of cirrhosis. *Gastrointest Endosc* 1996;43:568–571. [PubMed: 8781934]
4. Garcia-Tsao G, Boyer JL. Outpatient liver biopsy: how safe is it? *Ann Intern Med* 1993;118:150–153. [PubMed: 8416312]
5. Oberti F, Valsesia E, Pilette C, et al. Noninvasive diagnosis of hepatic fibrosis or cirrhosis. *Gastroenterology* 1997;113:1609–1616. [PubMed: 9352863]
6. Lu LG, Zeng MD, Wan MB, et al. Grading and staging of hepatic fibrosis, and its relationship with noninvasive diagnostic parameters. *World J Gastroenterol* 2003;9:2574–2578. [PubMed: 14606100]
7. Dodd GD 3rd, Baron RL, Oliver JH 3rd, et al. Spectrum of imaging findings of the liver in end-stage cirrhosis: part I, gross morphology and diffuse abnormalities. *Am J Roentgenol* 1999;173:1031–1036. [PubMed: 10511173]
8. Dodd GD 3rd, Baron RL, Oliver JH 3rd, et al. Spectrum of imaging findings of the liver in end-stage cirrhosis: part II, focal abnormalities. *Am J Roentgenol* 1999;173:1185–1192. [PubMed: 10541086]
9. Torres WE, Whitmire LF, Gedgaudas-McClees K, et al. Computed tomography of hepatic morphologic changes in cirrhosis of the liver. *J Comput Assist Tomogr* 1986;10:47–50. [PubMed: 3944316]
10. Child, CG.; Turcotte, JG. Surgery and portal hypertension. In: Child, CG., editor. *The Liver and Portal Hypertension*. Philadelphia, PA: Saunders; 1964. p. 50–64.
11. Pugh RNH, Murray-Lyon IM, Dawson JL, et al. Transection of the esophagus in bleeding oesophageal varices. *Br J Surg* 1973;60:648–652.
12. Bryce TJ, Yeh BM, Qayyum A, et al. CT signs of hepatofugal portal venous flow in patients with cirrhosis. *Am J Roentgenol* 2003;181:1629–1633. [PubMed: 14627587]
13. Landis J, Koch G. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–174. [PubMed: 843571]
14. Cosar S, Oktar SO, Cosar B, et al. Doppler and gray-scale ultrasound evaluation of morphological and hemodynamic changes in liver vasculature in alcoholic patients. *Eur J Radiol* 2005;54:393–399. [PubMed: 15899342]

15. Simonovsky V. The diagnosis of cirrhosis by high resolution sonography of the liver surface. *Br J Radiol* 1999;72:29–34. [PubMed: 10341686]
16. Dodd GD III, Baron RL, Oliver JH III. Enlarged abdominal lymph nodes in end-stage cirrhosis: CT-histopathologic correlation in 507 patients. *Radiology* 1997;203:127–130. [PubMed: 9122379]
17. Zhang XM, Mitchell DG, Shi H, et al. Chronic hepatitis C activity: correlation with lymphadenopathy on MR imaging. *Am J Roentgenol* 2002;179:417–422. [PubMed: 12130443]
18. Holloway BJ, Gore ME, A'Hern RP, et al. The significance of paracardiac lymph node enlargement in ovarian cancer. *Clin Radiol* 1997;52:692–697. [PubMed: 9313735]
19. Coakley FV, Hricak H. Imaging of peritoneal and mesenteric disease: key concepts for the clinical radiologist. *Clin Radiol* 1999;54:563–574. [PubMed: 10505992]

FIGURE 1.

Chart illustrating the diagnostic accuracy (presented as the mean AUC for 2 readers) and interobserver agreement (presented as the κ value for categorical variables and Pearson correlation coefficient* for continuous variables) of CT signs in the diagnosis of cirrhosis. CT signs are listed in order of decreasing AUC.

FIGURE 2.

A 56-year-old man with cirrhosis secondary to chronic viral hepatitis. Contrast-enhanced CT demonstrates nodularity of the diaphragmatic surface of the liver (arrow).

FIGURE 3.

A 45-year-old man with cirrhosis secondary to chronic viral hepatitis. CT without intravenous contrast demonstrates hypertrophy of the caudate lobe (arrow).

FIGURE 4.

A 50-year-old woman with cryptogenic cirrhosis. Contrast-enhanced CT demonstrates corkscrew vessels within the liver tissue (arrow).

FIGURE 5.

A 34-year-old man with cryptogenic cirrhosis. Contrast-enhanced CT demonstrates rounding of the left liver lobe tip (arrow).

FIGURE 6.

A 37-year-old man with cirrhosis secondary to chronic viral hepatitis. Contrast-enhanced CT demonstrates large-bowel wall thickening (arrows).

TABLE 1

Details of CT Technique for the Study Population

Parameter	Description	Cirrhotic (n = 67)	Noncirrhotic (n = 59)
Phases acquired	Portal venous only	27	12
	Portal venous and arterial	19	3
	Portal venous, early and late arterial	5	44
	Portal venous, early and late arterial, delayed	16	0
Collimation	1.25 mm	0	4
	2.5 mm	21	41
	3.75 mm	1	0
	5.0 mm	18	12
	7.0 mm	27	2

TABLE 2

Results of Univariate Analysis for the Diagnosis of CT Using a Variety of Morphological Findings

	Parameter	AUC (Reader 1)	AUC (Reader 2)	Interobserver Agreement (κ Values or Pearson Correlation Coefficient [*])
Hepatic	Overall impression	0.97	0.90	0.70
	Diaphragmatic surface nodularity	0.95	0.88	0.75
	Visceral surface nodularity	0.97	0.87	0.59
	Global or segmental volume loss	0.95	0.87	0.70
	Caudate hypertrophy	0.96	0.83	0.62
	Parenchymal heterogeneity	0.94	0.82	0.63
	Corkscrew vessels	0.90	0.75	0.50
Extrahepatic	Rounded left liver lobe tip	0.92	0.89	0.64
	Portosystemic varices	0.94	0.86	0.63
	Ascites	0.79	0.74	0.81
	Gall bladder wall thickening	0.87	0.82	0.62
	Small- or large-bowel wall thickening	0.89	0.81	0.65
	Short-axis portal vein diameter [*]	0.53	0.52	0.83 [*]
	Short-axis portal lymph node diameter [*]	0.85	0.85	0.78 [*]
	Craniocaudal splenic length [*]	0.86	0.83	0.83 [*]

Diagnostic accuracy is reported as AUC in receiver operating characteristic curve analysis. Interobserver agreement is reported as κ values (categorical variables) or Pearson correlation coefficients (continuous variables).

^{*} Observer agreement is given as Pearson coefficients, not κ values.