Original Paper

Diagnosis Performance of Different MR Imaging Signs of Cirrhosis: the Caudate to Right Lobe Ratio, the Posterior Right Hepatic Notch, and the Expanded Gallbladder Fossa

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ABSTRACT **Background & Aims** The purpose of the study is to evaluate the accuracy of the C/RL, RPN, and EGF in diagnosing cirrhosis. **Methods** The study population included 95 cirrhotic patients in the cirrhosis group (56 men, 39 women, age range 14-76;mean age 52.3) and 57 subjects in the control group (26 men, 31 women, age range 18-83;mean age 51). All MR examinations were performed by using the same protocol. Two radiologists independently assessed data sets in two different reading sessions. The sensitivity, specificity, and accuracy and the relative risk of the signs in diagnosing cirrhosis were calculated. The diagnosis accuracy of the C/RL sign was calculated using the ROC curve. The statistical significance of any difference of each sign between different classes of cirrhosis was also calculated. **Results** The interobserver agreement between the readers was excellent (κ≥ 0.81;95% CI:0.92, 1.0). There was a significant statistical difference of the diagnostic value of C/RL, RPN, and EGF between cirrhotic patients and control group ($p<0.001$). The sensitivity, specificity, and accuracy of C/RL were 72%, 87%, and 78%; 67%, 87%, and 75% for RPN; and 49%, 91%, and 65% for EGF. C/RL (OR=18.95) and RPN (OR=14.74) showed a higher risk for cirrhosis compared to EGF (OR=14.74). There was a statistical significance difference between C/RL and EGF ($p=0.002$) and between RPN and EGF for Child A class of cirrhosis (p-0.037). **Conclusion**The C/RL and RPN have similar performance regarding the diagnosis of cirrhosis having a higher diagnostic performance compared to EGF in cirrhosis.

KEY WORDS *Liver, Cirrhosis, Magnetic Resonance Imaging, Relative risk s*

Introduction

A definitive diagnosis of cirrhosis is made by means of histological findings after liver biopsy. However, taking into consideration the high incidence of virus hepatitis and liver cirrhosis, a significant number of patients undergo imaging examinations before the definitive diagnosis of cirrhosis has been established. Several studies (1-11) showed that morphological signs that can be identified on routine clinical imaging examinations often accompany cirrhosis. Therefore, knowing these signs as well as knowing the differences of their diagnostic performance in cirrhotic liver can be useful in clinical practice. Different morphological signs have been described on different imaging techniques (ultrasound, computer tomography, magnetic resonance imaging) including the transverse diameter of segment 4, caudate-to-right lobe ratio (C/RL), the right posterior notch (RPN), the right lobar atrophy, porta hepatis enlargement, and expanded gallbladder fossa (EGF). These morphological signs are the result of fibrosis accompanied by decreased blood flow within portal veins. The caudate-to-right lobe ratio is a quantitative measurement that demonstrated to have a high specificity and accuracy in diagnosing cirrhosis (5, 9). The size of the caudate lobe has been also correlated with the hepatic functional reserve in cirrhotic patients (12). It has been demonstrated that the caudate lobe was larger in patients with compensated cirrhosis than in patients with decompensated cirrhosis (12). However, the main disadvantage of this quantitative assessment is represented by the fact that is time consuming since several measurements of the caudate and right lobe must be calculated. Therefore these measurements are rarely done in daily clinical work and have not gained widespread use (1). The expanded gallbladder fosa (EGF) and the right posterior notch (RPN) are simple qualitative visual signs of cirrhosis (1, 2). Both findings showed a high specificity and a high positive predictor value for the MR diagnosis of cirrhosis (1, 2). Despite of their low sensitivity, these signs can be routinely used in clinical practice (1, 2). To our knowledge, a comparison between the C/RL, EGF, and RPN in cirrhotic liver has not been studied. The purpose of this study was to evaluate and to compare the

diagnosis performance of these signs in diagnosing cirrhosis.

Methods

Study population

Our institutional medical database was cross-referenced to identify all consecutive patients who underwent MR imaging for suspected liver lesions or for evaluation of the severity of liver cirrhosis during a 15-month period. One hundred twenty-five cirrhotic patients and 165 non-cirrhotic patients underwent MR imaging. Cirrhotic patients were retrospectively included in the study if they had pathologically proved cirrhosis. The patients with hepatocellular carcinoma larger than 2 cm and the patients who undergone hepatic resection or therapeutic interventional procedures (e.g. ablation, chemoembolization) were not included in this study. Finally, 95 cirrhotic patients were included in the cirrhosis group (Table 1).

Table 1. The cirrhotic patients included in the study population.

Cirrhotic group				Underlying cause of cirrhosis											Child-Pugh classification			
	No	Age range (years)	Mean age (years)	HCV[1]	HBV[2]	HBV and ethanol	Ethanol	HBV and HDV[3]	HCV and ethanol	HBV and HCV	Toxic	Autoimmune	Primary sclerosing cholangitis	Unknown	A	B	C	Unknown
Female	39	14-67	52	11	7	0	0	2	0	0	1	2	2	14	22	12	1	4
Male	56	17-76	52.4	10	9	6	5	3	4	3	4	0	0	12	24	16	7	9
Total	95	14-76	52.23	21	16	6	5	5	4	3	5	2	2	26	46	28	8	13

[1] hepatitis C virus infection
[2] hepatitis B virus infection
[3] hepatitis D virus infection

In the control group were included patients who fulfilled the following criteria: no history of chronic liver diseases and no previous hepatic or biliary surgery. The patients with focal liver lesions greater than 2 cm were also not included in this study since the presence of those lesions might modify the liver shape and consequently might influence the interpretation criteria. The control group consisted of 57 subjects (26 men, 31 women, age range 18-83; mean age 51). Institutional review board approval with waived informed patient consent was obtained for this retrospective study.

MR Imaging Protocol

All MR examinations were performed using a 1.0-T MR system (Gyroscan Intera, Philips Medical Systems, Netherlands). For optimal signal reception, a surface body-coil was used, covering the entire liver. The imaging protocol included a transverse respiratory-triggered, non-enhanced T2-weighted turbo spin-echo (TSE) sequence [repetition time (TR)/echo time (TE)= 1600ms/100ms, flip angle 90˚, matrix size 256*512, field-of-view 37-42*50-71cm, section thickness 7mm and intersection gap 1.0mm] and a breath-hold, transverse non-enhanced T1-weighted fast-field echo (FFE) sequence in- and out-of-phase [TR/TE=15ms/6.9ms for in-phase acquisition and TR/TE=15ms/3.45ms for out-of-phase acquisition; flip angle 25°, 1 NSA, matrix size 256x256, field of view 37-42x50-71cm, section thickness 7mm and intersection gap 1.0mm] were acquired.

After acquisition of the non-enhanced sequences, Gadobutrol (Gadovist®, Bayer Schering Pharma AG, Berlin, Germany) was injected intravenously at a dose of 0.1mmol per kilogram of bodyweight with a flow rate of 2mL/sec followed by a 20mL saline flush at the same flow rate using a power injector (Spectris®, Medrad, Indianola, Pa, USA). Dynamic gradient-recalled MR imaging was timed to capture the arterial, portal venous and equilibrium phase and was performed with a fast-field echo (FFE) sequence [TR/T 5.1ms/1.69ms, flip angle 25°, matrix size 208*256, field of view 37-43*44-50cm, section thickness 4.2mm]. There were no adverse reactions noted in any of our patients.

Image Analysis

Two radiologists (with 6 and 4 years of experience in abdominal MRI, respectively) independently assessed data sets in two different reading sessions (1, the evaluation of the presence or absence of RPN; and 2, the presence or absence of EGF). To reduce any bias, reading sessions were separated by 4-week intervals and data sets were analyzed in random order from both cirrhotic patients and control subjects. The evaluation of both readers was made by using the non-enhanced T1 weighted images and dynamic gradient-recalled MR images. Both readers were blinded to all clinical patient data.

In the first reading session, the readers were asked to define the presence or absence of RPN and in the second reading session, the readers were asked to define the presence or absence of EGF. In both assessments it was used a 2-point grading scale: 0- absence of the sign; 1-presence of the sign. Both readers were asked to evaluate these qualitative signs by using the same criteria. The RPN was defined as a sharp indentation in the right posterior surface of the liver (1) (Fig 1) and the EGF is represented by the enlargement of the pericholecystic space (Fig 2). Space is bounded laterally by the edge of the right hepatic lobe, medially by the edge of the lateral segment of the left lobe (2). The medial segment of the lateral lobe should not be seen on the same axial image.

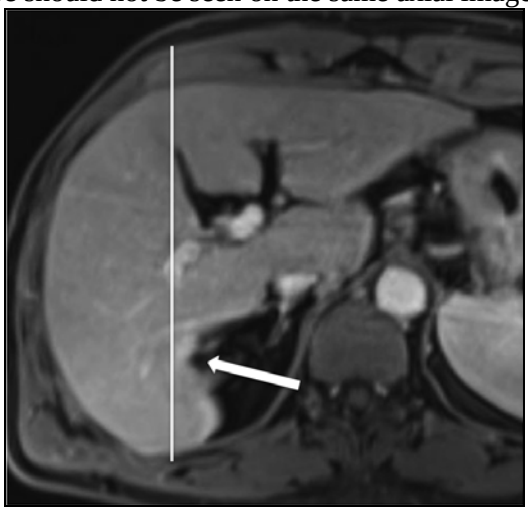

Fig 1. 56-year-old man with liver cirrhosis Child A. Axial enhanced MR image (15/3.45, 25° flip angle). The C/RL is high (1.37) and the RPN is easily identified (arrow). Note the fact that the sharp notch that defines RPN and represents the landmark of the caudate lobe is situated on the line through the bifurcation of the right portal vein.

Fig 2. Axial contrast-enhanced FFE MR image (5.1/1.69, 25° flip angle). The enlargement of the pericholecystic space (star). Space is bounded laterally by the edge of the right hepatic lobe, medially by the edge of the lateral segment of the left lobe.

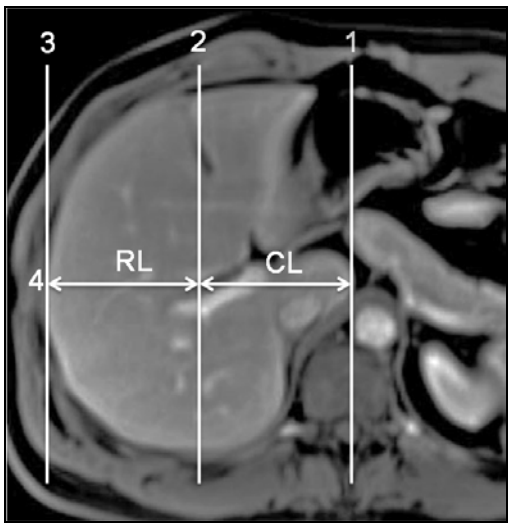

Fig 3. Axial contrast-enhanced FFE MR image (5.1/1.69, 25° flip angle) obtained during the portovenous phase at the level of right portal vein bifurcation shows the method of calculating C/RL (9). Line 1, line 2, and line 3 are parallel to the midsagittal plane. Line 1 is drawn through the medial margin of the caudate lobe. Line 2 is drawn through the right lateral wall of the bifurcation of the right portal vein and line 3 is drawn through the most lateral margin of the right lobe. The widths of the caudate and right lobe are calculated on line 4. Line 4 is perpendicular to line 1 and is situated at midway between the posterior wall of the main portal vein and the anterior wall of the inferior vena cava. CL – the width of the caudate lobe. RL – the width of the right lobe.

The C/RL (the width of the caudate lobe / the width of the right lobe) was calculated by one radiologist (6 years experience in abdominal MRI). The reader chose images for measurement on the basis of the clarity of the portal veins on enhanced dynamic gradient-recalled MR images. The measurements were made by using the bifurcation of the right portal vein as the landmark of the caudate lobe (9) (Fig 3).

Statistical Analysis

Descriptive results regarding the presence or absence of RPN and EGF were reported in relative numbers. Interobserver agreements between the readers were assessed using Cohen's kappa test. A kappa value of 0 indicated poor agreement, a value of 0.01-0.20 slight agreement, a value of 0.21-0.40 fair agreement, a value of 0.41-0.60 moderate agreement, a value of 0.61-0.80 good agreement, and a value of 0.81-1.00 implied an excellent agreement (13). A *p*-value of less than 0.05 was considered statistically significant. The qui-square test was used to evaluate the statistical difference of the diagnostic value of the signs between cirrhotic group and control group. The diagnosis accuracy of the signs was calculated.

The diagnosis accuracy of the C/RL sign was calculated by using the ROC curve. The sensitivity and specificity of the C/RL sign for diagnosis of cirrhosis were calculated having a cut-off point of 0.50. The relative risk (odds ratio) of C/RL, EGF and RPN for the diagnosis of cirrhosis was also calculated. The statistical significance of any difference between the three signs in diagnosis of cirrhosis was calculated using Friedman and Wilcoxon test and the statistical significance of any difference of each sign between different Child-Pugh classes of cirrhosis was calculated using Kruskal-Wallis and student *t* test . All statistical analyses were performed by using commercially available software (SPSS 13.0, Chicago, IL).

Results

The interobserver agreement between the 2 readers was excellent ($\kappa \geq 0.81$; 95% CI: 0.92, 1.0) in the evaluation of the presence or absence of RPN and EGF.

Table 2. Summary of the diagnostic performance of the C/RL, the RPN, and the EGF and the relative risk of all three morphological signs in the diagnosing cirrhosis. The cut-off value for C/RL was 0.50.

Sign	Number of subjects with morphological signs within the control group (57 subjects)	Number of cirrhotic patients with morphological signs within the cirrhotic group (95 patients)	Sensitivity%	Specificity%	Accuracy%	Odds ratio
C/RL	7	69	72	87	78	18.95
RPN	7	64	67	87	75	14.74
EGF	5	47	49	91	65	10.18

Table 3. The statistical differences between C/RL, RPN, and EGF in different classes of cirrhosis.

	Child-Pugh A	Child-Pugh B	Child-Pugh C
	p-value	*p-value*	*p-value*
C/RL - RPN	0,229	0,537	0,685
C/RL - EGF	0,002	0,083	0,451
RPN - EGF	0,037	0,255	0,197

There was a significant statistical difference of the diagnostic value of C/RL, RPN, and EGF between cirrhotic patients and control group ($p<0.001$). Table 2 summarizes the sensitivities, specificities, accuracies, and the relative risk of C/RL, RPN, and EGF for cirrhosis with regard to the diagnosis of cirrhosis. The ROC curve of the C/RL is shown in Fig 4. There was no statistical significant difference between C/RL and RPN (p=0,382) for the diagnosis of cirrhosis (Fig 1). There were statistical significant differences between C/RL and EGF (p=0,000) and between RPN and EGF (p=0,010) for the diagnosis of cirrhosis (Fig 5). There was a statistical significance difference between C/RL and EGF and between RPN and EGF for Child A class of cirrhosis (Table 3).

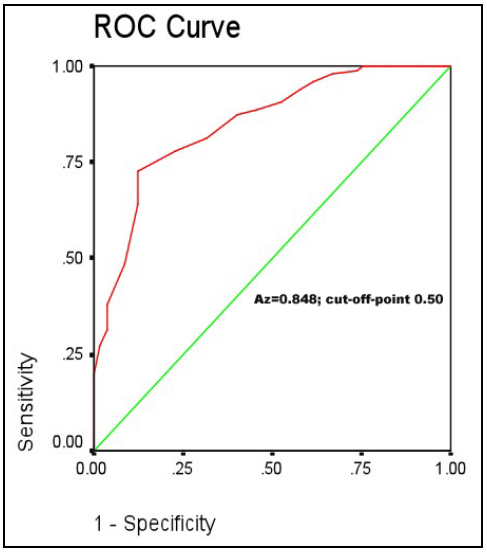

Fig 4. The ROC curve of the C/RL in diagnosing cirrhosis.

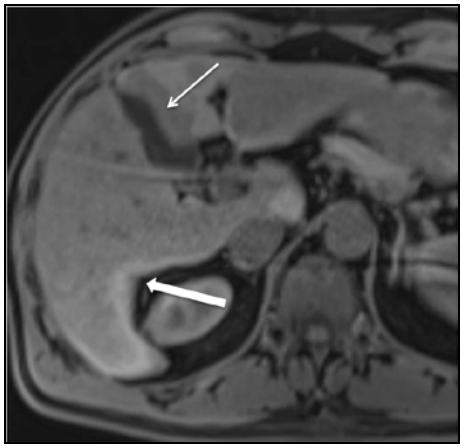

Fig 5. 42-year-old woman with liver cirrhosis Child B. Axial unenhanced MR image (15/3.45, 25° flip angle) shows the right posterior hepatic notch (large arrow). On the same image the EGF is not present. The pericholecystic space is bounded medially by the edge of the medial segment of the left lobe (small arrow) and not by the lateral segment.

Discussion

Cross-sectional imaging has been used for the diagnosis of cirrhosis based on the quantitative evaluation of lobar changes of the liver as well as on qualitative findings such as the right posterior hepatic notch and the expanded gallbladder fossa. In cirrhotic liver there is an atrophy of the right

lobe concomitant with a hypertrophy of the caudate lobe due to alterations in portal blood flow and hepatic fibrosis (14). Regardless the compensated or uncompensated type of cirrhosis the caudate lobe is larger in these patients compared with the noncirrhotic patients (12). Harbin et al (4) have shown that on ultrasonography or CT examinations the cirrhotic livers can be differentiated from noncirrhotic livers by using C/RL with a sensitivity of 84%, a specificity of 100%, and an accuracy of 94%. In their study, the C/RL was calculated by using the main portal vein bifurcation as the landmark of the caudate lobe.

However, Awaya et al (9) have proposed a modified C/RL for the quantitative evaluation of cirrhotic liver. Based on the fact that the caudate lobe receives blood supply from the posterior segmental branch in 51% of the cases (15) and the intrahepatic course of the caudate branches is short and less influenced by fibrosis (16), the authors have considered that the landmark of the caudate lobe should be the bifurcation of the right portal vein. Comparing the ROC curve of the C/RL described by Harbin with Awaya's modified ratio for diagnosing cirrhosis there was a significant higher Az value for modified C/RL (0.797; p=0.040) than for Harbin's ratio (Az=0.737) (9). In our study we used the C/RL modified by Awaya and we obtained an Az value of 0.848 for the diagnosis of cirrhosis. The different Az values may be the result of the fact that the patients included in Awaya's study were reported having only mild or moderate cirrhosis in 65% of cases (9). When we calculated the sensitivity, the specificity, and the accuracy of C/RL having a cut-off point of 0.50 we obtained a sensitivity of 72%, specificity of 87%, and accuracy of 78%. Our results are different from those reported by Harbin. Since the Az value of the C/RL used in our study has shown higher values comparing with Harbin's results, we would have been expect that the sensitivity, the specificity, and the accuracy would have been higher. However, in their study (4) the authors have used different landmarks for C/RL and different criteria for including cirrhotic patients and control subjects. Harbin did not specify the underlying cause of cirrhosis and patients with diffuse liver diseases were also included in the control group. These differences may account for the different accuracies in the studies.

The evaluation of the C/RL requires performing contrast-enhanced cross sectional imaging in order to identify the portal vein bifurcations. Moreover, several measurements are needed for obtaining this ratio. Therefore, the method gained limited use in clinical practice for assessment of cirrhotic patients. The right posterior hepatic notch and the expanded gallbladder fossa are two simple qualitative visual findings for cirrhosis (1, 2). Ito et al (1) described the RPN as a sharp indentation on the posteroinferior liver surface different from the renal impression. The presence of the RPN in cirrhosis is the result of the atrophy of the right lobe and hypertrophy of the caudate lobe (1). Thus, both signs, C/RL and RPN, are dependent on the same lobar changes of the liver. This may be the reason why the diagnostic sensitivity, specificity, and accuracy together with odds ratio of each sign are similar in our study. When comparing the signs, we did not find any statistical significance difference between them for the diagnosis of cirrhosis. Moreover, there was no difference between these signs in the diagnosis of different classes of cirrhosis. The sensitivity, specificity, and accuracy of RPN were reported by Ito to be 72%, 98%, and 82%, respectively (1). Our results show lower values (sensitivity 67%, specificity 87%, and accuracy 75%). The RPN is a morphological sign more frequently seen in patients with alcoholic cirrhosis compared with patients with viral cirrhosis since the volume index of the caudate lobe is significant greater in alcoholic cirrhosis than in viral cirrhosis (10). In our study population there was included only a small percentage of patients with alcoholic cirrhosis (5%). In comparison, in the study of Ito (1), 13% of the patients included in their study were with alcoholic cirrhosis. This difference in the patient population together with the fact that the RPN is statistically more frequent in the alcoholic type of cirrhosis might explain the differences in the diagnosis performances between the two studies.

In contrast to C/RL and RPN, the expanded gallbladder fossa is a sign that reflects different segmental liver changes in a cirrhotic liver. Although, the hypertrophy of the caudate lobe and atrophy of the right lobe contribute to the presence of EGF, another two segmental changes have an important role in the visualization of the sign: the atrophy of the medial segment of the left hepatic lobe and the cephalocaudal enlargement of the lateral segment of the left hepatic lobe (2). The atrophy of the segment 4 in cirrhotic liver has been demonstrated by Lafortune (3) who showed that regardless the cause or the severity of cirrhosis, the mean diameter of the segment 4 measured on ultrasonography is significant decreased in cirrhosis compared with normal liver.

Torres et al (17) demonstrated on a volumetric evaluation of the cirrhotic liver a decrease in volume by 10.9% of the medial segment of the left lobe when compared with normals. On the other hand, the enlargement of the lateral segment of the left hepatic lobe is seen only in compensated viral induced cirrhosis whereas in decompensated cirrhosis there is an atrophy of this segment (8). It has been also demonstrated that the left lobe does not increase in volume with the progression of the cirrhosis in contrast to the right lobe which shows a significant decrease in volume (11). There is also a marked variability in the volumetric measurements of the lateral segment of the left lobe in normal livers (18). These variations of the left lobe volume can be responsible for the low sensitivity (49%) and low odds ratio (OR=10.18) of EGF. The low sensitivity of this sign in our study has been previously reported (1, 2). However, the specificity of EGF in this study is high (91%) and comes to confirm the results of other authors (2). When comparing EGF with C/RL and RPN, there was a statistical significance difference between the last two signs and EGF in diagnosing cirrhosis ($p<0.010$). These results suggest that the EGF is a useful sign in evaluation of cirrhosis when is used in conjunction with other morphological findings reported in previous studies (2, 5, 9, 10, 19).

Our study results demonstrated a significant statistical difference between C/RL and EGF ($p=0.002$) and between RPN and EGF ($p=0.037$) for Child A class of cirrhosis. No differences were found between signs for Child B and Child C classes of cirrhosis ($p>0.05$). These data might express that in compensated and less severe clinical cirrhosis the morphological changes are mainly represented by the hypertrophy of caudate lobe and atrophy of the right lobe.

The following limitations of our study need to be address. We did not evaluate the diagnosis performance of combined C/RL, RPN, and EGF. However, we tried to assess the individual role of each sign in the diagnosis of cirrhosis. Consideration of two findings or of all three signs of cirrhosis would improve the diagnosis accuracy. Another limitation is represented by the fact that we did not correlate the morphological signs with the underlying cause of cirrhosis. Further studies are needed to determine if these signs might help to differentiate the cirrhosis induced by different causes. A potential criticism of this study may also be the exclusion of the patients with chronic liver diseases including fibrosis. A relevant evaluation would involve an assessment of the morphological findings in cirrhotic patients in comparison with the findings in patients with chronic liver diseases. Finally, the C/RL, the RPN, and the EGF cannot be only calculated and visualized on MR liver examinations. Contrast-enhanced CT enables the evaluation of all three signs. However, MR examinations is at this moment extensively used in the evaluation of cirrhosis since this method offer a more accurate and complete evaluation of the cirrhotic liver.

In conclusion, the caudate to right lobe ratio and the right posterior hepatic notch have similar performance regarding the diagnosis of cirrhosis. The expanded gall-bladder fossa is a sign with low sensitivity and high specificity and represents an important additional finding of cirrhosis.

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