ORIGINAL ARTICLE

Magnetic resonance cholangiography compared with endoscopic retrograde cholangiography in the diagnosis of primary sclerosing cholangitis

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Background: Magnetic resonance cholangiography (MRC) has gained popularity for diagnosing primary sclerosing cholangitis (PSC). We determined the accuracy of MRC compared with endoscopic retrograde cholangiography (ERC) for diagnosing PSC. **Materials and Methods:** This retrospective case-control study was conducted on patients referred to an outpatient gastroenterology clinic from 2001 to 2013. Patients with established diagnosis of PSC who had undergone MRC and ERC within a 6-month interval were included. Controls were selected from patients who had undergone imaging for reasons other than PSC evaluation. Disease outcome at the study time and liver biochemistry data at diagnosis and 1-year thereafter were retrieved. Diagnostic accuracy of MRC in comparison with ERC was evaluated. **Results:** A total of 46 definite PSC patients (age at diagnosis = 36.8 ± 11.6 years, 33 male) were found. Diagnostic imaging for PSC was ERC alone in 12, MRC alone in 23, and ERC plus MRC in 11 patients. Controls were 89 patients mostly with bile stones. The sensitivity, specificity, and positive and negative likelihood ratios of MRC was 90.9%, 95.5%, 20.23, and 0.10, respectively. Early PSC was found more frequently by MRC compared with ERC (30.4% vs. 8.3%, $P = 0.146$). No significant difference was found between imaging modalities with regards to patients' outcome ($P = 0.786$) or liver biochemistry at diagnosis or 1-year thereafter ($P > 0.05$). **Conclusion:** Starting diagnostic imaging for PSC with MRC seems better and may provide diagnosis of PSC at its earlier phase. Further studies with larger sample of patients and longer follow-ups are warranted.

Key words: Cholangiography, diagnosis, magnetic resonance imaging, sclerosing cholangitis, sensitivity, specificity

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INTRODUCTION

Primary sclerosing cholangitis (PSC) is a rare cholestatic liver disease that is characterized by bile duct destruction due to chronic inflammation and obliterative fibrotic changes resulting in bile stasis and hepatic fibrosis.[1] Up to 80% of the PSC cases are associated with inflammatory bowel disease (IBD), mostly ulcerative colitis.[2] Among IBD patients, PSC is more likely to be asymptomatic at presentation, and when symptomatic, they are not always specific. Anatomic changes of the bile ducts are even present before alteration in liver biochemistry. As a result, many PSC cases are diagnosed when the disease is in advanced phase.[3] With no effective medical treatment available yet, PSC in many cases will progress to cirrhosis and end-stage liver disease, and >50% of the PSC patients will need liver transplantation within 10-15 years of symptom development.[1,2]

The endoscopic retrograde cholangiography (ERC) is the current standard imaging method which, in a typical case, shows multifocal areas of stricturing of intra and/or extra-hepatic bile ducts, with intervening segments of normal or dilated ducts.[4] However, an increase in routine testing of liver biochemistry and improved noninvasive imaging techniques such as magnetic resonance cholangiography (MRC) has resulted in PSC being diagnosed earlier than previously; before cholangiography shows a severe generalized beading of the biliary tree and stenosis. Although PSC often has a long and unpredictable course, early detection of PSC can alter the clinical course of the disease by treating severe strictures and evaluating dominant strictures to find early cholangiocarcinoma.[2]

The MRC has recently gained popularity for diagnosing PSC. In this regard, studies suggested that the accuracy of MRC may be comparable with or even superior to ERC. In a recent meta-analysis of available data, MRC had a sensitivity of 86% and specificity of 94% in comparison to ERC in diagnosing PSC. Accordingly, MRC may be sufficient for diagnosis of PSC in many cases, and the risks and costs associated with ERC can be avoided.[5] Based on our anecdotal experience

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in a referral gastroenterology clinic with a total of 715 registered IBD patients, being routinely tested for liver biochemistry with high suspicious for detecting early PSC, we hypothesized that MRC may be sufficiently sensitive for diagnosing PSC. In our experience, we found that minor changes including minimal irregularities of the bile duct wall and minor variation of bile duct diameters, which are usually reported normal by some radiologists, are in fact early signs of PSC in patients at risk for the disease. These early findings are usually not detected by ERC. Therefore, we aimed to determine the accuracy of MRC in comparison with ERC in the diagnosis of PSC.

MATERIALS AND METHODS

Patients and settings

This retrospective case-control study was conducted on patients referred to a single outpatient gastroenterology clinic from 2001 to 2013. Patients with established diagnosis of PSC based on cholangiographic appearances, laboratory data, and clinical course were included. Those patients who had undergone MRC and ERC within a 6-month interval were included into the case group. Controls were identified similarly from patients who had undergone MRC and ERC for reasons other than PSC evaluation. Patients with history of Whipple surgery and liver transplant patients were not included into the study. The study was approved by the Ethics Committee of the Isfahan University of Medical Sciences and consent was obtained from PSC patients for retrieving and re-evaluating their imaging documents.

Assessments

A total of 3,710 patients' documents from the clinic and also 1,573 documents from our ERC database were evaluated to find patients with and without PSC, who had undergone both ERC and MRC. All ERC procedures had been done and reported by a single gastroenterologist with about 14 years of interventional ERC experience. MRC studies were re-evaluated by the gastroenterologist and a radiologist with 21 years of faculty experience who was not aware to the ERC results or patients' clinical history.

Patients' documents were evaluated for final disease outcome at the time of study and interview was done in case that it was needed. Liver biochemistry data at the time of PSC diagnosis and 1-year thereafter were retrieved.

Statistical analysis

Data were analyzed using the SPSS (SPSS Inc., Chicago, IL., USA) software for windows version 16.0. Quantitative and qualitative data are reported as mean ± standard deviation and number (%), respectively. Comparison between groups was done using Chi-square test for qualitative data and Mann-Whitney U-test for quantitative data, because data were not normally distributed based on the Kolmogorov-Smirnov test. Sensitivity, specificity, positive and negative predictive values and likelihood ratios of MRC for the diagnosis of PSC in comparison with ERC were calculated. $P < 0.05$ was considered as significant.

RESULTS

A total of 64 PSC patients were found. Evaluating these cases resulted in 46 definite PSC cases with age at diagnosis of 36.8 ± 11.6 years and including 33 male patients. There were 39 patients with IBD, including 26 patients with ulcerative colitis and 13 with Crohn's disease. Diagnosis of IBD has been done after the diagnosis of PSC in 3 patients. Five patients also found to have cholangiocarcinoma carcinoma. Diagnostic imaging for PSC was ERC alone in 12, MRC alone in 23, and ERC plus MRC in 11 patients. There was only one PSC diagnosis with small bile duct injury based on liver biopsy, but with normal MRC. Also one patient who had bile duct stone without clear radiographic evidence of PSC in his first ERC had a follow-up ERC indicating PSC after 5-month. In 8 patients, the first MRC had been reported normal by radiologists, but was reported suspicious for early PSC by the gastroenterologist according to minor changes detected in the imaging [Figures 1 and 2]. Follow-up MRC studies (up to 2 years) approved the PSC diagnosis in 6 patients. Patients with both ERC and MRC imaging available were included into the study as the case group. Furthermore, a total of 89 patients were found to have undergone ERC and MRC with <6-month interval for reasons other than PSC evaluation mostly bile stones. These patients were included into the study as the control group.

Magnetic resonance cholangiography was indicative for PSC in 10 from 11 patients in the case group resulting in a sensitivity of 90.9% (95% confidence interval [CI]: 58.6-98.4%). In the control group, 3 patients have been

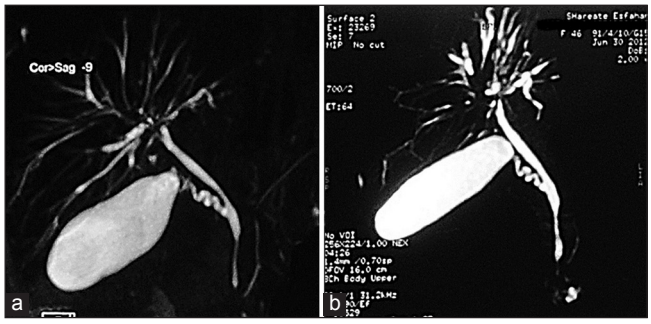

Figure 1: Early primary sclerosing cholangitis (PSC) versus typical PSC after 2 years in a 45-year-old female with ulcerative colitis and elevated results of liver function tests. (a) Coronal magnetic resonance cholangiopancreatography (MRCP) image shows a mild intrahepatic ductal narrowing and irregularity, and a subtle stricture at the bifurcation of left and right hepatic ducts (arrow). (b) Coronal MRCP image with suspicious PSC demonstrate multifocal strictures and irregularity of the intrahepatic bile ducts with secondary proximal intrahepatic duct dilatation with some irregularity mimicking beaded appearance

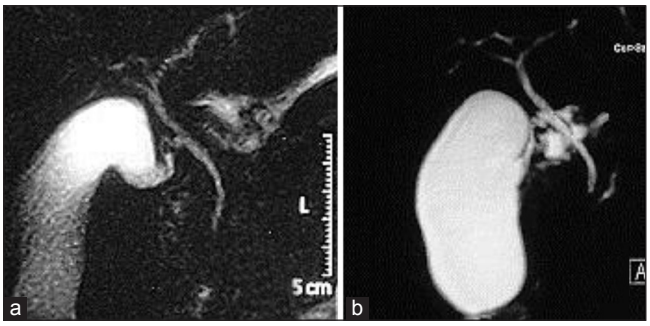

Figure 2: Early primary sclerosing cholangitis (PSC) in a 31-year-old man with jaundice and abdominal pain (a) coronal magnetic resonance cholangiopancreatography image show Mild irregularity and narrowing mostly in right lobar branches. However these changes can overlook (b) follow-up imaging after 4 years, more evident intrahepatic narrowing and dilatation with beaded appearance are shown in favor of early PSC

reported to have irregularities in bile ducts suspicious for PSC but not approved by ERC, and one other patient with PSC diagnosis in the report was found to have no PSC in ERC evaluation. Further follow-up of the patient has not been conclusive for PSC diagnosis. The specificity of MRC accordingly was calculated as 95.5% (95% CI: 88.8-98.7%) [Table 1]. The positive and negative predictive values were calculated as 71.4% (95% CI: 41.9-91.4%) and 98.8% (95% CI: 93.6-99.8%). The positive and negative likelihood ratios were calculated as 20.23 (95% CI: 7.62-53.67) and 0.10 (95% CI: 0.01-0.62), respectively.

Comparison of imaging modalities for diagnosing PSC in terms of patients' outcomes is summarized in Table 2. Early PSC was found more frequently by MRC compared with ERC (30.4% vs. 8.3%), though it was not statistically significant ($P = 0.146$). No significant difference was found between imaging modalities with regards to patients' outcome or liver biochemistry at diagnosis or 1-year thereafter [Table 2].

Table 1: Diagnostic accuracy of MRC compared with ERC in diagnosis of PSC

Test result	ERC+	ERC−
MRC+	10 (90.9)	4 (4.4)
MRC−	1 (9.0)	85 (95.5)

Data are presented as *n* (%); ERC = endoscopic retrograde cholangiography; MRC = Magnetic resonance cholangiography; PSC = primary sclerosing cholangitis

Table 2: Comparison of imaging modalities for diagnosing PSC in terms of patients' outcomes and liver biochemistry

Outcomes	ERC (*n* = 12)	MRC (*n* = 23)	*P*
Early PSC	1 (8.3)	7 (30.4)	0.146*
Outcome			
Controlled disease	6 (50)	12 (52.1)	0.786*
Uncontrolled disease	4 (33.3)	6 (26.0)	
Liver transplantation	1 (8.3)	3 (13.0)	
Death	1 (8.3)	2 (8.6)	
AST at diagnosis	116.1±104.8	123.1±208.7	0.470†
AST after 1-year	36.6±16.1	33.7±19.6	0.661†
ALT at diagnosis	135.8±106.5	193.1±313.5	0.914†
ALT after 1-year	35.0±11.7	37.8±34.9	0.443†
ALP at diagnosis	837.6±546.7	586.6±515.6	0.178†
ALP after 1-year	513.6±341.6	331.0±219.9	0.234†

Data are presented as mean ± SD or *n* (%); SD = Standard deviation; PSC = Primary sclerosing cholangitis; ERC = Endoscopic retrograde cholangiography; MRC = Magnetic resonance cholangiography; AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; ALP = Alkaline phosphatase; *Chi-square test, †Mann-Whitney U-test

DISCUSSION

The aim of the present study was to determine the accuracy of MRC in comparison with ERC in the diagnosis of PSC. In general, MRC has been used more frequently than ERC for the diagnosis of ERC in our practice. The results of our study showed high sensitivity (90.9%) and specificity (95.5%) as well as high negative (98.8%) but not positive (71.4%) predictive values for MRC in diagnosing PSC. These findings are similar to most of the previous studies that has shown sensitivity as 77-97% and specificity as 64-100% for MRC in diagnosing PSC.[6-10] A recent meta-analysis by Dave *et al*. on six studies with 456 subjects (185 with PSC) showed a pooled sensitivity and specificity of MRC for PSC detection as 86% and 94%, respectively, and positive and negative likelihood ratios as 15.3 and 0.15, respectively,[5] similar to our findings (positive and negative likelihood ratios of 20.23 and 0.10). Also, cost-effectiveness analyses suggest that an initial MRC examination, with selective use of ERC in the following, would be a cost-effective approach for diagnosing PSC.[11,12] Hepatic magnetic resonance imaging, in addition to diagnosis of PSC, can provide information about the status of the liver which is important in diagnosing cholangiocarcinoma and also pretransplant evaluation in these patients.[13] According to acceptable sensitivity and high negative predictive value, therefore, starting diagnostic imaging with MRC seems reasonable. Although MRC is better than ERC in demonstrating dilated ducts above an obstruction, it may not be able to precisely determine the length of strictures below the obstructed duct. Hence, and as the positive predictive value is not high, ERC should remain the final diagnostic imaging in case there is any doubt in the diagnosis or if confirmation or the precise evaluation of disease severity is needed or endoscopic therapy or tissue samplings are required.[1]

In addition to our main findings, we also found a number of PSC patients with minor changes in MRC and approved PSC at follow-up imaging. Minimal irregularities of the bile duct wall and minor variation of bile duct diameters are usually reported normal by many radiologists unless high clinical suspiciousness is raised. In patients with abnormal liver biochemistry and at increased risk for PSC (IBD patients), these minor changes may be early inflammatory

phase of PSC.[1] Although the smooth branched bile ducts is a good clue to normality of biliary tree, it seems that minor changes in bile ducts may be seen in biliary spasm, but such changes may disappear in ERC using high pressure dye injection. These spasms are probably induced by patchy inflammations occurring in PSC cases. Accordingly, MRC may be a better imaging modality for diagnosing early PSC than ERC; however, further studies are needed to approve this finding. While our study was retrospective and we were not able to work on MRC images quality, future prospective studies can provide better information in this regard with the possibility of more qualified MRC images by the improving the techniques.

Although previous studies have tried to compare diagnostic accuracy of MRC in comparison with ERC for PSC, there is a lack of data on clinical consequences of applying each of these imaging modalities.[5] We compared those patients for whom the diagnosis has been made only by ERC comparing with MRC. Although MRC was better than ERC in detecting PSC at its early phase, we found no significant difference between imaging modalities regarding patients' outcome or liver biochemistry 1-year after diagnosis. Longer follow-up and larger population, however, is needed to find possible different clinical course with earlier diagnosis and treatment with today's drugs. Finding new therapies that may postpone biliary tract fibrotic changes increases the importance of early PSC detection. It should be noted that the sample size of our study was limited and our study was retrospective prone to selection bias. Hence, prospective randomized studies are required in this regard and also to provide more precise data to prove MRC as the gold standard for the diagnosis of PSC rather than ERC.

Our study has some limitations including retrospective design and limited sample size of the case group. We included only one reader for each imaging modality, and though previous studies showed very good inter-observer agreement for the diagnosis of PSC, inter-observer variability was still possible in our study. Also, because patients from the case and control group had different types of disease, we were unable to calculate positive and negative predictive values accurately.

CONCLUSIONS

In summary and based on our study results, starting diagnostic imaging for PSC with MRC is better and may provide diagnosis of PSC at its earlier phase. However, our study results should be interpreted cautiously considering the study limitations. The ERC should remain the final diagnostic imaging in case there is any doubt in the diagnosis or if confirmation is needed or if therapeutic intervention is predicted. Future studies with larger sample of patients and also comparing the effect of using each of the ERC and MRC imaging modalities for early diagnosis and the effect on patient outcome are warranted.

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AUTHOR'S CONTRIBUTIONS

MHE generated the idea and participated in designing the study and gathering data. HA, MSJ, and AH participated in designing the study and gathering data. RS participated in gathering data and drafting the manuscript with HA and MSJ. All authors studied, revised, and approved the final version of the manuscript.

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