

Ultrasound versus Magnetic Resonance Cholangio-Pancreatography in the Diagnosis of Suspected Extra-hepatic Intrinsic Biliary Obstruction

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Abstract

Background	Evaluation of obstructive jaundice is a common clinical problem.
Objective	To compare diagnostic accuracy, sensitivity and specificity of ultrasound and Magnetic Resonance Cholangio-Pancreatography in the diagnosis of intrinsic obstructive biliary disease.
Methods	One hundred and sixty patients with an obstructive jaundice for whom ultrasound (U/S), magnetic resonance imaging (MRI) and Magnetic Resonance Cholangio-Pancreatography (MRCP) were performed. The final diagnosis was confirmed by surgery, tissue biopsy and/or Endoscopic Retrograde Cholangio-Pancreatography (ERCP) in some cases.
Results	Of the 164 patients, 102 (62.2%) were found to have choledocholithiasis, 42 patients (25.6%) with benign stenosis and 20 patients (12.2%) had cholangiocarcinomas. Regarding choledocholithiasis, U/S examination showed a diagnostic accuracy of 80.15% with sensitivity of 71.08% and a specificity of 95.83 %. Conversely, MRCP showed a diagnostic accuracy of 93.89%, sensitivity of 93.97% and a specificity of 93.75 %. Regarding benign stenosis: U/S showed a diagnostic accuracy of 78.62% with a sensitivity of 16.67 % and a specificity of 97.29%. The diagnostic accuracy of MRCP was 93.13%, with a sensitivity of 90% and a specificity of 94.05%. In malignant stenosis: of the 20 patients with cholangiocarcinomas, 6 were localized in the upper third or hilar biliary tract (Klatskin tumor), 4 in the mid third and 10 in the distal third of the common bile duct (CBD). The diagnostic accuracy of US in malignant stenosis was 93.13%, with a sensitivity of 61.12% and a specificity of 98.23%. For MRCP, the diagnostic accuracy in detecting malignant stenosis was 93.89%, with a sensitivity of 72.23% and specificity of 97.34%. In all cases, no difference was noticed when comparing US and MRCP.
Conclusion	Lithiasis was the most common cause of extra-hepatic intrinsic biliary obstructions. U/S is considered the first choice option in the diagnostic imaging of obstructive disease. If laboratory and clinical findings are supported by U/S, ERCP is required for therapeutic purposes, or if necessary surgery is performed. Ultrasound is highly reliable for ruling out benign stenosis, though not for demonstrating their presence. MRCP is required only for staging of malignant stenosis, or if the suspicion posed by clinical and laboratory findings is not confirmed at U/S.
Key words	Ultrasound, MRCP, extra-hepatic intrinsic biliary obstruction.

Introduction

Evaluation of obstructive jaundice is a common clinical problem. Often, the initial problem is to distinguish between intrahepatic and extrahepatic biliary obstruction⁽¹⁾. Extra-hepatic Biliary obstruction may be due to a variety of causes including choledocholithiasis, tumors (pancreatic head cancer,

ampullary cancer, and cholangiocarcinoma), and trauma, including injury after gall bladder surgery, with choledocholithiasis being the most common cause⁽²⁾. Many studies have shown that clinical data such as history, physical examination, and laboratory tests can accurately identify up to 90% of patients whose jaundice is caused by extrahepatic obstruction⁽³⁻¹¹⁾.

Although history, laboratory investigations and imaging techniques may help to differentiate benign from malignant biliary strictures, it remains a clinical challenge⁽¹²⁾.

The assessment of extra-hepatic obstruction often require the use of various imaging modalities to confirm the presence, level and cause of obstruction and aid in treatment planning. The various imaging modalities can be classified into direct and indirect techniques⁽¹³⁾.

The former are more invasive, and include ERCP and Percutaneous Transhepatic Cholangiography (PTC). They carry a higher associated risk, but have the added ability to sample tissue and perform therapeutic maneuvers, such as biliary drainage with stenting or stone removal⁽¹⁴⁻¹⁶⁾, but with risk of morbidity 1-7% such as pancreatitis, cholangitis, perforation, bleeding and biliary leak, and mortality rate of 0.2-1.0 % and unsuccessful cannulation of the ducts in 3-9%⁽¹⁷⁻²⁰⁾. Also, direct techniques are limited to the evaluation of the intrinsic biliary tract and cannot define the presence of extrinsic compression of the biliary tree by surrounding structures. Indirect techniques such as Ultrasound, CT scan and MRCP improve image quality while at same time maintain a low risk profile⁽¹⁾.

Trans-abdominal ultrasound is the first-line imaging investigation in patients with jaundice or right upper-quadrant pain⁽²¹⁻²³⁾. Dilated ducts are usually taken as indirect evidence of biliary obstruction. The presence of normal ducts, however, does not exclude obstruction⁽²³⁾; this is mainly because biliary obstruction may not be accompanied by dilatation of the CBD, conversely, the CBD increases in diameter in response to cholecystectomy and aging⁽²⁴⁻²⁷⁾. Despite these exceptions, ductal dilatation remains an excellent clue to biliary obstruction. Specifically, ultrasound has been shown to be highly accurate (78-98%) for detecting extra-hepatic biliary obstruction⁽¹⁾.

Magnetic Resonance Cholangio-Pancreatography (MRCP) is widely performed as a primary imaging modality for the assessment of obstructive jaundice and other benign or

malignant bilio-pancreatic ducts abnormalities. The primary MRCP application is the evaluation of biliary obstructions due to choledocholithiasis, iatrogenic strictures, cholangiocarcinoma or pancreatic carcinoma⁽²⁸⁾.

The objective of the study is to compare the diagnostic accuracy, sensitivity and specificity of ultrasound and MRCP in patients with suspected intrinsic biliary obstruction.

Methods

This prospective study was done on 164 patients (76 males and 88 females) with an age range 24-70 years (mean age is 56 years) suffering from obstructive jaundice in Al-Imamian Al-Kadhimiyan Medical City from June 2010 to October 2012.

All the patients included in this study had clinical and laboratory findings suggestive of obstructive jaundice (biliary colic, jaundice, increase of serum bilirubin level above the normal limit of 2 mg/dl), all the patients being referred to radiology department by general surgeon or gastroenterologist after full clinical and laboratory examination. All the patients underwent US and MRCP examination. Any patients with positive clinical and laboratory findings of obstructive jaundice and negative ultrasound examination were excluded from the study.

Ultrasound examination: All the examinations were performed with a convex multi-frequency probe of 3-5 MHz (HD 11XE, Philips medical system). The US study was done in the supine position after adequate period of fasting for at least 6-8 hours. The ultrasound findings were classified into 3 categories: Biliary stones, benign stenosis (revealed as smooth tapering of the biliary ducts) and malignant stenosis (Irregular or eccentric wall thickening or intraluminal vegetations or isoechogenic mass, associated with an abrupt interruptions and dilatation of the biliary tree).

MRI examination: All MRI examinations were performed with 1.5 Tesla system (MAGNETOM Avanto, Siemens medical system) also after enough period of fasting for at least 6 hours.

MRCP protocol consisted of axial and coronal images (source images), and post processing of these images by means of MIP reconstruction, so as to obtain optimal visualization of the biliary tree. The mean performance time was 20-25 minutes. MRCP findings were also classified into 3 categories: biliary stones (seen as endoluminal round or oval-shaped filling defects with low intensity signal, surrounded by the high signal intensity of the bile), benign stenosis (smooth and concentric or showed distal convexity and gradual and symmetric caliber restriction) and (malignant stenosis (characterized by an abrupt irregular and eccentric interruption of the biliary tract with upper abnormal dilatation and lower regular caliber were considered malignant).

The final diagnosis of all the patients was proved by ERCP, surgery and histopathology and the results of ultrasound and MRCP were compared. Test performance characteristics: Statistical analysis was performed using the program SPSS (version 11 for Microsoft window). Statistical significance was assumed at level of ($P < 0.05$). The sensitivity is the conditional probability that a diseased person has a positive test results. Its value can be changed by changing the cutoff point for positive test results. The specificity is the conditional probability that a disease free person has a negative test results. Positive predictive value (PPV) is the conditional probability that a person with a positive test results is truly diseased. Its value depends on the cutoff for positive test result and the prevalence of the disease in the screened population. Negative predictive value (NPV), is the conditional probability that a person with a negative test results is truly free of the disease.

Results

Of the 164 patients 102 (62.2%) were found to have choledocholithiasis, 42 patients (25.6%) with benign stenosis and 20 patients (12.2%) had cholangiocarcinomas

Regarding choledocholithiasis, ultrasound examination showed a diagnostic accuracy of 80.15% with sensitivity of 71.08% and a specificity of 95.83 % (Table 1). Four false

positives were due to abnormal refraction of the wall. The 24 false negative were related to calculi of less than 2mm in size located in the distal area and/or to the patients' morphological type. Conversely, MRCP showed a diagnostic accuracy of 93.89%, sensitivity of 93.97% and a specificity of 93.75 % (Table 1). The 6 false positive were due to a small cholangiocarcinoma in the distal area in 1 patient and 1 inflammatory stenosis in the ampulla in the other 2 patients, which were considered calculi. The 4 false negatives were due to pneumobilia (intra-ductal air bubbles) disguising a stone in 2 patients, and in the other 2 due to calculi of less than 3mm. There is statistically insignificant difference between U/S and MRCP in choledocholithiasis ($P = 0.286$). Fig. 1 shows U/S and MRCP images in 37 years old female with CBD stone.

Benign stenosis: of the 42 patients with benign stenoses, 22 showed an iatrogenic stenosis as a result of laparoscopic cholecystectomy (in 14 patients), gastric resection (in 2 patients), bilio-enteric anastomosis (in 2 patients), and after ERCP (in 4 patients). Six had an obstructive cholangitis, and 14 patients had stenosis in the ampullary region resulting from inflammation and benign tumors. Ultrasound showed a diagnostic accuracy of 78.62% with a sensitivity of 16.67 % and a specificity of 97.29% (Table 1). The 4 false positive were recorded due to misdiagnosis of a malignant stenosis. On the 24 false negative were due to difficulties of the ultrasound in the visualization of distal CBD. The diagnostic accuracy of MRCP was 93.13%, with a sensitivity of 90% and a specificity of 94.05% (Table 1). The 6 false positive were due to misdiagnosis of a malignant stenosis in 2 patients and microlithiasis and dilatation of main pancreatic duct in the other 4 patients. The 4 false negative were due to artifacts from magnetic susceptibility, overlapping surgical clips and bowel gas, which prevent identification of benign stenosis. In benign stenosis comparing ultrasound and MRCP a statistically significant difference was not obtained ($P = 0.999$). Fig. 2 shows ultrasound and MRCP images in 42 years old female with benign stricture in the CBD.

In malignant stenoses: of the 20 patients with cholangiocarcinomas, 6 were localized in the upper third or hilar biliary tract (Klatskin tumor), 4 in the mid-third and 10 in the distal third of the CBD. The diagnostic accuracy of ultrasound in malignant stenosis was 93.13%, with a sensitivity of 61.12% and a specificity of 98.23% (Table 1). The 4 false positive were due to benign stenosis considered malignant, while 8 false negatives were due to a malignant stenosis misinterpreted as extrinsic compression. For MRCP, the diagnostic accuracy in detecting malignant stenosis was 93.89%, with a sensitivity of 72.23%

and specificity of 97.34% (Table 1). The 4 false positives were due to misdiagnosis of benign stenosis considered malignant, whereas the 4 false negative were due to a small stenosis in 2 patients, and in the other 2 due to overlap artifacts (surgical clips and bowel gas). Comparison of ultrasound and MRCP, the analysis of data did not show a statistically significant difference ($P = 0.635$). Fig. 3 shows 2 MRCP images in 2 different patients with malignant stricture in the distal and proximal CBD.

Table 1. Diagnostic accuracy, sensitivity and specificity of MRCP and US in Cholelithiasis, benign stenosis and malignant stenosis

Feature	Stone		Benign stenosis		Malignant stenosis	
	U/S	MRCP	U/S	MRCP	U/S	MRCP
Number	102	102	42	42	20	20
True +ve	74	92	14	32	8	12
False -ve	24	4	24	4	8	4
False +ve	4	6	4	6	4	4
Diagnostic accuracy (%)	80.1	93.89	78.62	93.13	93.13	93.89
Sensitivity (%)	71.08	93.97	16.67	90	61.12	72.23
Specificity (%)	95.83	93.75	97.29	94.05	98.23	97.34
PPV (%)	94.87	93.88	77.78	84.21	66.67	75
NPV (%)	72.09	93.93	83.56	96.83	94.73	97.3
<i>P</i> value	0.286		0.999		0.635	

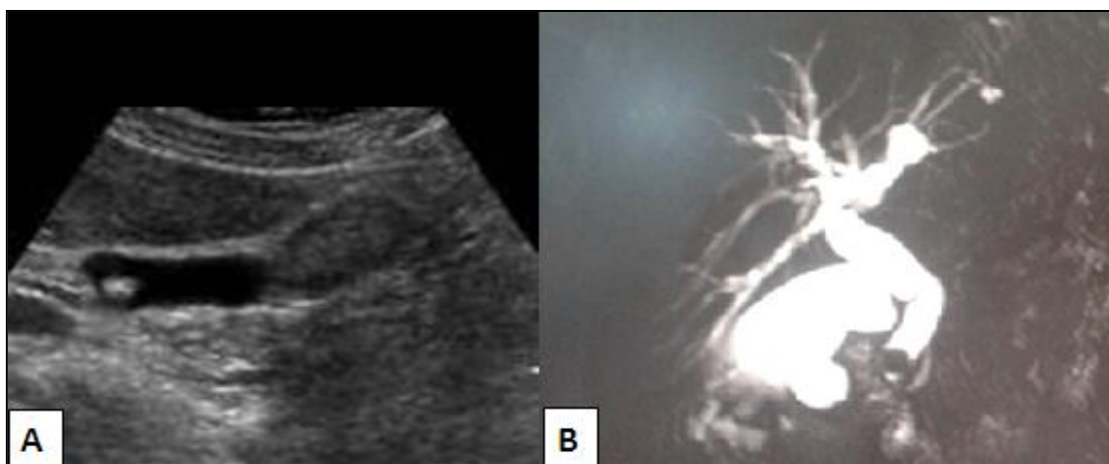


Fig. 1. 37 years old female presented with obstructive jaundice caused by stone in the CBD. A: U/S image and B: MRCP image

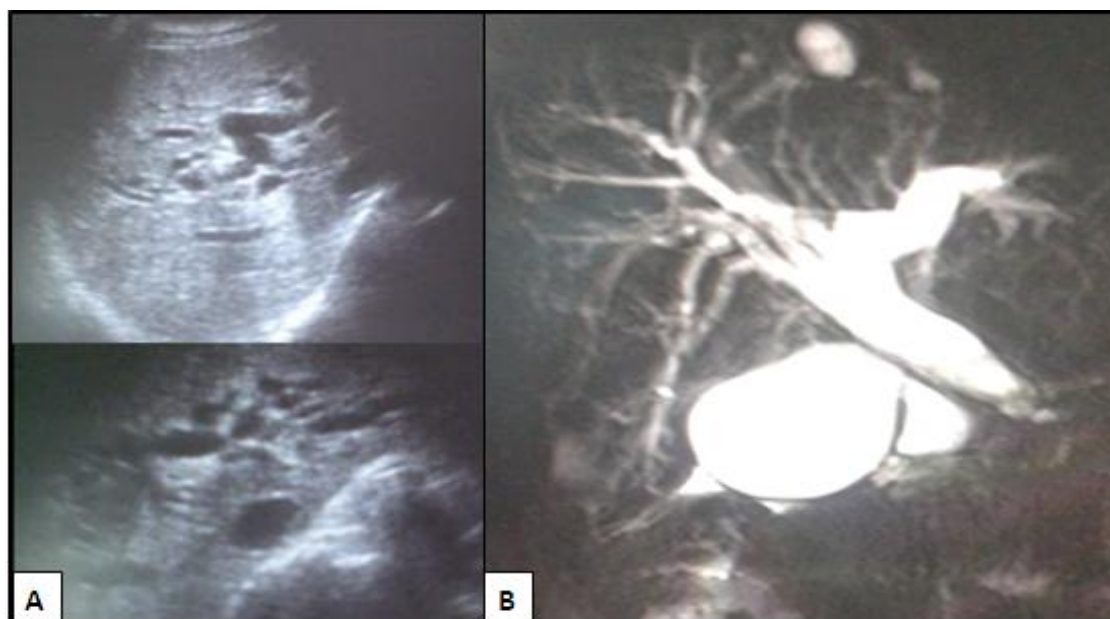


Fig. 2. 42 years old female presented with obstructive jaundice caused A: U/S image show dilated intra-hepatic & extra-hepatic bile ducts. B: MRCP image show dilated intra-hepatic & extra-hepatic bile ducts with smooth tapering at the distal part of the CBD. This case is proved to be benign stricture in CBD

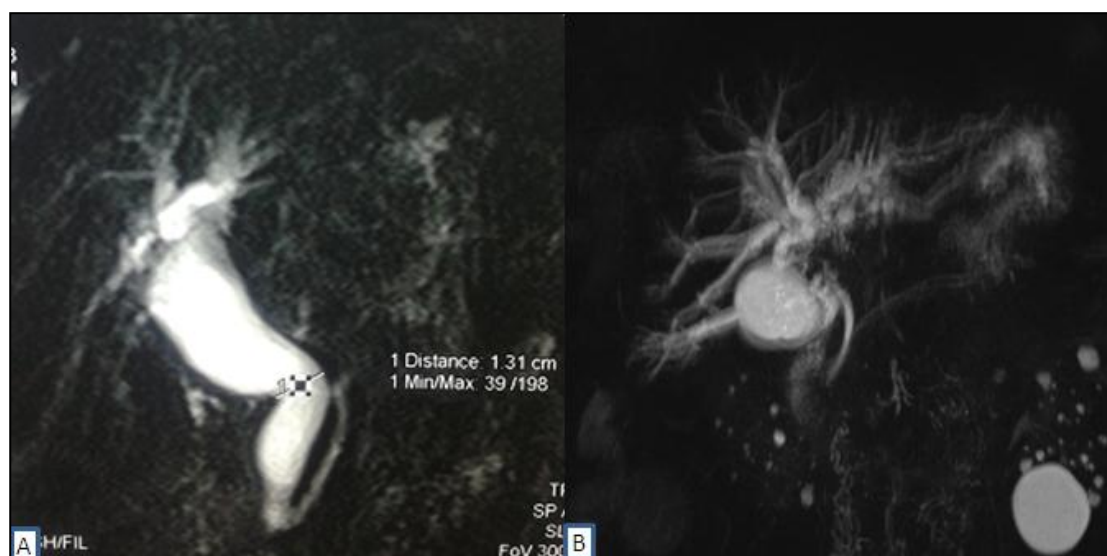


Fig. 3. MRCP in 2 different patients with malignant stricture due to cholangiocarcinoma. A: 54 years old male with distal CBD stricture. B: 62 years old male with proximal CBD stricture

Discussion

Jaundice is a common problem in medical and surgical gastroenterological practice. The surgical jaundice can be caused by the obstruction of the bile duct as with gall stones, strictures, malignancy, such as cholangiocarcinoma (in which the jaundice is persistent

and progressive), periampullary carcinoma, carcinoma gall bladder and carcinoma head of pancreas. Obstructive jaundice is common amongst females and Choledocholithiasis is the commonest benign cause⁽²⁹⁾.

Ultrasound is the imaging tool of choice for evaluation of the biliary system and is accurate

in diagnosing cholelithiasis in 97% of cases⁽³⁰⁾. Previously reported studies showed a sensitivity range of 20-80%⁽³¹⁻³⁴⁾; these wide ranges of differences in sensitivity among various case series are partially attributable to the impossibility of approaching the distal CBD and ampullary region in obese patients and patients with abdominal meteorism, as well as to the variability of the US technique applied. The high sensitivity in our case series presumably derived from the change in patient's morphology and quality of the device. Since our data show that U/S and MRCP have the same diagnostic potential in choledocholithiasis, the purpose of US is to select candidates for therapeutic ERCP without proceeding to MRCP⁽³³⁾. In our opinion, however, MRCP should only be applied for the correction of possible false negative cases from ultrasound. MRCP, for its high diagnostic value, is necessary in patients showing equivocal clinical and laboratory findings and negative U/S prior to performing ERCP, which is invasive procedure. Our data on MRCP diagnostic accuracy, sensitivity and specificity are comparable to the previously reported literature^(32,35-41), the lowest figures for sensitivity, reported by Little et al⁽³²⁾ and Stiris et al⁽³⁵⁾ were due to their initial inexperience in accurately detecting small calculi in the distal CBD, and not to the limitations of MRCP.

MRCP and ultrasound virtually resolve almost all diagnostic problems, and have therefore considerably restricted the role of diagnostic ERCP. Although most authors make no distinction among the types of biliary stenosis, we subdivided them into malignant and benign stenosis, and the diagnostic value of the imaging techniques was assessed for each type, also considering that clinical and laboratory findings frequently overlap at disease onset.

The analysis of data in benign stenosis shows how diagnostic result for MRCP overlap, whereas US is highly reliable for ruling out benign stenosis, though not for demonstrating their presence. In our U/S study of benign stenosis, we obtained fair accuracy, high specificity and low sensitivity. The high

specificity was attributable to the capability of U/S to detect true negatives in benign stenosis, thus showing the cause of the obstruction by calculi or malignant stenosis. The low sensitivity figures are to be related to intrinsic limitations of the methodology, which, though showing the indirect signs of stenosis^(38,42), do not allow for optimal visualization of the distal CBD and the ampullary region, which is where benign stenosis are often localized. However, our comparison of U/S and MRCP reveals overlapping performance, though MRCP performed better in detecting true positives. MRCP's diagnostic accuracy, sensitivity and specificity are always high and higher than those reported by Arslan et al⁽⁴³⁾, who compare MRCP and ERCP in 78 patients with obstruction and reported a sensitivity and specificity of 86.4% and 82.4% respectively for benign stenosis.

In our study, MRCP and U/S performed on an equal level in detecting true negatives and positives in malignant stenosis. In the literature, the majority of U/S studies on malignant stenosis demonstrate a high sensitivity, and specificity and diagnostic accuracy, though-in contrast to our study- extrinsic and intrinsic causes of obstruction are examined together. Sharma et al⁽⁴⁴⁾ obtained a sensitivity and specificity for U/S of 94% and 96% respectively; these high figures are attributed to the prevalence of patients with GB carcinoma and pancreatic head carcinoma. Chamberlain et al⁽⁴⁵⁾ reported a sensitivity of 93% and specificity of 99% for U/S in the identification of the obstruction site and portal involvement when occurring. Bloom et al⁽⁴⁶⁾ reported a sensitivity and specificity of 98% and these high figure because both intra- and extra-hepatic cholangiocarcinomas are included in this study. In our study, US showed high diagnostic accuracy and specificity and relatively low sensitivity. These low values were presumably related to the small dimension of some cholangiocarcinomas (only showed by dilatation of the biliary ducts at US) and /or there localization in the distal CBD, a region of difficult approach for US. Our data on MRCP can be

compared with those reported on malignant stenosis by Arslan⁽⁴³⁾ (sensitivity of 88.6% and a specificity of 94.1%) and slightly lower than those by Little et al⁽³²⁾ (diagnostic accuracy, sensitivity and specificity of 97%,93% and 100%), Lomas et al⁽³⁶⁾ (sensitivity of 100% and specificity of 98%) and Hussein et al⁽³⁸⁾ (sensitivity and specificity of 100%); it must be born in mind that Lomas and Hussein do not make a distinction between benign and malignant stenosis. Our low sensitivity figures (72%) were due to the presence of small cholangiocarcinomas. Liang et al⁽⁴⁷⁾ showed the diagnostic accuracy of MRCP in malignant obstruction was 82.9%, and MRCP was found to have high diagnostic specificity for determining the location and extent of obstruction.

In conclusion, the most common cause of extra-hepatic intrinsic biliary obstruction was choledocholithiasis. Ultrasound is still the first choice imaging procedure of biliary obstructive disease, as it can shape the subsequent diagnostic and therapeutic approach, its high specificity, above MRCP in cases of lithiasis, allows patients to be referred directly for either ERCP or surgery. However, owing to its low sensitivity in most of the benign stenoses and distal CBD disease, where the clinical and laboratory suspicion is strong and unsupported by ultrasound and/or in the presence of conditions affecting ultrasound performance, and for a thorough staging evaluation of malignancy, MRCP is required.

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