Predictive value of ultrasonography and magnetic resonance cholangiopancreatography in the diagnosis of biliary obstruction

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OBJECTIVE: *Use of diagnostic tools with high predictive value for common biliary duct (CBD) obstruction has the potential to provide valuable information. This study aimed to examine the respective diagnostic values of biochemistry, abdominal ultrasonography (US), and magnetic resonance cholangiopancreatography (MRCP) in patients with suspected biliary obstruction.*

MATERIALS AND METHODS: *A total of 119 patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) based on a suspicion of CBD obstruction were included. Patients also had data for biochemical and hematologic tests, abdominal US and MRCP. The respective sensitivity, specificity, negative predictive value, and positive predictive value of US, MRCP, and the laboratory parameters in the diagnosis of ERCP-confirmed CBD obstruction were estimated.*

RESULTS: *ERCP did not show obstruction in 15.1% of the cases. Based on 95% confidence intervals, MRCP had greater sensitivity than ultrasound in predicting obstruction (95% vs. 62%). In addition, ultrasound had a very high 31.9% false negative rate when compared to MR (4.2%). On the other hand, a combined approach had better diagnostic value. None of the laboratory parameters exhibited a predictive value. However, old age was significantly associated with biliary obstruction.*

CONCLUSION: *MRCP, particularly when combined with ultrasound, is a useful diagnostic tool for the diagnosis of common biliary duct obstruction and may have the potential to eliminate the need for further ERCP in some patients. On the other hand, US alone does not seem to have acceptable diagnostic value. Further large and prospective studies are warranted to draw firm conclusions.*

KEY WORDS: Biliary Obstruction, Endoscopic Retrograde Cholangiopancreatography (ERCP), Magnetic Resonance Cholangiopancreatography (MRCP), Ultrasonography

Introduction

Biliary obstruction is defined as the blockage of the bile ducts that may occur anywhere along the path from the

liver to the intestinal tract. Globally, it represents a major health problem associated with significant morbidity and mortality.

The most common clinical manifestation of the gallstones is the dilatation of the common bile duct (CBD), which comprises the extrahepatic biliary system. Gall stones represent the most prevalent cause of biliary obstruction in the Western world, affecting approximately 5% to 25% of adult individuals; furthermore, 5% of the patients undergoing cholecystectomy were found to have simultaneous occurrence of CBD stones [1]. Obstruction of the CBD may lead to a number of complications including

cholangitis, jaundice, secondary biliary cirrhosis or pancreatitis. In addition, it be can associated with significant morbidity and even mortality, when CBD stones remains in place for long durations of time [2]. Thus, use of diagnostic tools with high predictive value for CBD obstruction would provide valuable information for surgeons before the onset of such pathologies [3].

First-line diagnostic work up for CBD obstruction includes biochemical laboratory parameters and abdominal ultrasonography (US) [4]. However, the predictive value of these investigations for CBD stones is limited. According to the most recent NICE (National Institute for Clinical Excellence) guidelines, a magnetic resonance cholangiopancreatography (MRCP) should be performed in patients with suspected biliary obstruction [3,5], based on its well established diagnostic capabilities as a non-invasive method that does not require the use of ionizing-radiation.

Endoscopic retrograde cholangiopancreatography (ERCP), perioperative common-bile duct exploration and intraoperative cholangiography are the gold standard methods for detecting CBD stones. Among these, ERCP, in addition to its diagnostic role, also has role in the treatment. Published studies have already established the high sensitivity and specificity of this method in detecting biliary obstruction, although it is also associated with considerable morbidity (5-6%) and mortality (0.01-0.89%) [6,7].

The main purpose of this study was to examine the respective predictive values of biochemistry, abdominal US, and MRCP for ERCP-confirmed biliary obstruction, in an effort to question the routine requirement for ERCP in all cases.

Materials and Methods

PATIENTS

A total of 119 patients who underwent ERCP based on a suspicion of CBD obstruction between February 2017 and August 2019 were included. Eligible patients had available data for demographic parameters, biochemical and hematologic tests, abdominal US and MRCP, and were examined for the presence of CBD obstruction. Subjects less than 16 years of age and those who underwent ERCP for indications other than possible cholestatic obstruction were excluded. The respective diagnostic values of US, MRCP and the laboratory parameters were compared against ERCP, which is considered the gold standard technique in the diagnosis of the obstruction of the common bile duct.

ASSESSMENTS

Demographical data and laboratory assessments
The following demographic and laboratory data were retrospectively collected: age and gender; serum liver function tests (LFT) including direct bilirubin (reference range: 0.01-0.2 mg/dL), total bilirubin (0.3-1.2 mg/dL), alkaline phosphatase (ALP; 30-120 IU/L), alanine transaminase (ALT; 1-35 IU/L), aspartate aminotransferase (AST; 1-35 IU/L) and γ-glutamyltransferase (GGT; <55 IU/L); serum C-reactive protein (CRP; <5 mg/L); white blood cell (WBC; 4.37-9.68 mcL); serum lipase (< 67 U/L); serum amylase (28-100 U/L). All measurements were done at a single central laboratory using similar kits.

ULTRASONOGRAPHY

Transabdominal ultrasonography was performed by means of a Vivid 4 portable ultrasound unit (GE, Medical System, Waukesha, WI, USA) equipped with a convex low-MHz transducer with a bandwidth of 1-5 MHz (GE Voluson 730) and a linear high-MHz transducer with a bandwidth of 5-7 MHz (GE Voluson 730) in all patients to assess the entire gallbladder and biliary duct. All sonographic examinations were independently performed by one of our two clinically experienced radiologists with at least 10 years of clinical experience in abdominal sonography.

MRCP

Patients fasted for 4-hours prior to the study in order to reduce fluid secretions within the stomach and duodenum, reduce bowel peristalsis, and promote gallbladder distension. We do not routinely use anti-peristaltic agents in such cases. All MRCP scans were performed on a Siemens-wide bore Verio scanner (Siemens Healthcare, Malvern, PA, USA) at 3T, using a combination of a body matrix coil and spine matrix coil. Sequences performed included 6-mm coronal and axial fat-saturated T2 Haste single breath hold sequences of the entire liver, axial DWI (ep2diff, b = 50, 400, 1000), T1 fl2d axial 6-mm imaging, fat-saturated T2 haste 4-mm axial imaging through the CBD, fat-saturated coronal T2 Haste 40-mm thick slabs and a respiratory triggered coronal 3D T2 weighted SPACE volumetric acquisition.

ERCP

ERCP procedures were performed with side-viewing duodenoscopes (JF-260V; TJF-260V, Olympus, Japan). Biliary cannulation was attempted with a standard cannula catheter or sphincterotome. The cannulation method (such as wire cannulation or direct cannulation) was left at the discretion of the ERCP endoscopist, based on the clinical condition of the patient. For common bile duct cannulation, a 0.025-in (VisiGlide 2 guidewire,

Olympus, Japan) or 0.035-in (Dreamwire, Boston Scientific) guidewire was used, when wire cannulation was required. Then, the diluted contrast material (7mL Urografin from Bayer Company, Spain, with 3mL normal saline) was injected.

All US and MRCP images were interpreted by a senior radiologist with special interest in hepatobiliary imaging. In addition, all ERCP procedures were performed by an experienced endoscopist.

On MRCP and US imaging, a diameter of CBD > 7 mm was considered an indication of obstruction. On ERCP, presence of dilatation >7 mm and direct visualization of obstruction was interpreted as CBD. Absence of dilated CBD precluded a diagnosis of obstruction, even in the presence of a mass lesion.

Statistical analysis

Data were analyzed using IBM SPSS Statistics version 20.0 software (SPSS Inc., Chicago, IL). Descriptive data are presented in number (percentage) or mean ± standard deviation, where appropriate. Normality was tested using both hypothesis tests and graphical methods. The significance of the intergroup difference for continuous variables were tested using student t test or Mann-Whitney U test, depending on the distribution of the data. For age and biochemical measurements, receiver operator characteristic curves (ROC) were generated to examine the predictive role of these continuous parameters and potential cut-off values. Diagnostic parameters including sensitivity, specificity, positive predictive value, and negative predictive values were calculated for ultrasonography, MR cholangiopancreatography and age in predicting biliary obstruction confirmed by ERCP. Non-overlap of 95% confidence intervals considered indication for significant difference between diagnostic performance parameters (sensitivity, specificity, negative predictive value, positive predictive value). A p value smaller than 0.05 was considered the indication for statistical significance.

Results

Table I shows demographical data and obstruction etiology as confirmed by ERCP. ERCP did not show obstruction in 15.1% of the cases. The most common cause for obstruction was choledochal stone, which was present in more than half of the patients, followed by choledochal sludge (7.6%) and stricture
Table II shows diagnostic parameters for ultrasound and MR cholangiopancreatography in predicting biliary obstruction confirmed by ERCP. Based on 95% confidence intervals, MR cholangiopancreatography had greater sensitivity than ultrasound in predicting obstruction (95% vs. 62%). In terms of other diagnostic per-

TABLE I - *Demographical data and etiology of obstruction**

Characteristics	
Age, y (mean±SD)	56.3±17.9
Female gender	76 (63.9%)
Etiology of obstruction	
No obstruction	18 (15.1%)
Choledochal stone	62 (52.1%)
Choledochal sludge	9 (7.6%)
Stricture	9 (7.6%)
Periampullary tumor	6 (5.0%)
Peripapillary diverticula	5 (4.2%)
Odditis	3 (2.5%)
Others†	7 (5.9%)

Unless otherwise stated, data presented as n (%).
*Based on ERCP findings.
†cholangiocarcinoma, cholangitis, choledochal cyst, pancreatitis, protruded papilla

formance parameters, the differences did not reach statistical significance, although ultrasound had numerically higher specificity and MR cholangiopancreatography had numerically better negative predictive value. In addition, ultrasound had a very high 31.9% false negative rate when compared to MR (4.2%), indicating that almost one third of positive cases will be missed when only ultrasound is used. Sensitivity, specificity, positive predictive value, and negative predictive value of a combined approach (i.e. when obstruction findings with at least one of the methods was considered indication for obstruction) are shown in the rightmost colon of Table 2. Combined approach had a better negative predictive value than ultrasound alone: 0.80 (0.44-0.96) vs. 0.28 (0.17-0.43), with a relatively low false negative rate (1.7%).

Based on ROC analysis, AUC values for predicting ERCP confirmed biliary obstruction for total bilirubin, direct bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, lipase, amylase, white blood cell count, and c-reactive protein were 0.488, 0.479, 0.444, 0.450, 0.415, 0.493, 0.504, 0.494, 0.564, and 0.560, respectively; indicating no predictive value. In addition, there was no difference between patients with and without biliary obstruction in terms of these biochemical parameters (p>0.05 for all comparisons) (Table III). However, patients with biliary obstruction were significantly older than patients without (59.0±17.0 vs. 41.4±16.2 years, p<0.001). Age had a potential predictive value on ROC analysis with AUC 0.771. An optimal cut-off value of 51 years of age yielded the following: sensitivity, 0.69 (95% CI, 0.59-0.78); specificity, 0.78 (0.52-0.93); positive predictive value, 0.95 (0.86-0.98); and negative predictive value 0.31 (0.19-0.47), but with a high false negative rate (68.8%).

TABLE II - *Diagnostic parameters for ultrasound and MR cholangiopancreatography in predicting biliary obstruction confirmed by endoscopic retrograde cholangiopancreatography*

	Ultrasound	MRCP	Combined
True positive rate	63 (52.9%)	96 (80.7%)	99 (83.2%)
True negative rate	15 (12.6%)	9 (7.6%)	8 (6.7%)
False positive rate	3 (2.5%)	9 (7.6%)	10 (8.4%)
False negative rate	38 (31.9%)	5 (4.2%)	2 (1.7%)
Sensitivity	0.62 (0.52-0.72)	0.95 (0.88-0.98)	0.98 (0.92-0.99)
Specificity	0.83 (0.58-0.96)	0.50 (0.27-0.73)	0.44 (0.22-0.67)
Positive predictive value	0.95 (0.86-0.99)	0.91 (0.84-0.96)	0.91 (0.83-0.95)
Negative predictive value	0.28 (0.17-0.43)	0.64 (0.36-0.86)	0.80 (0.44-0.96)

Numbers in parenthesis denote 95% confidence intervals.

TABLE III - *Biochemical values for patients with and without biliary obstruction*

Biochemical parameter	Obstruction absent (n=18)	Obstruction present (n=101)	p
Total bilirubin, mg/dl	2.2±2.5	2.0±2.5	0.870
Direct bilirubin, mg/dl	1.2±1.9	1.0±1.5	0.781
Alkaline phosphatase, U/L	166.4±104.0	140.7±67.6	0.452
Aspartate aminotransferase, U/L	56.2±42.1	48.3±36.4	0.500
Alanine aminotransferase, U/L	91.1±88.5	63.3±58.8	0.252
Gamma-glutamyl transferase, U/L	111.4±98.1	105.4±84.8	0.926
Lipase, U/L	78.5±100.0	67.3±90.7	0.953
Amylase (U/L)	109.3±97.3	103.7±108.6	0.935
White blood cells, x103/mm3	8.2±3.3	8.5±3.0	0.390
CRP, mg/L	50.1±73.4	45.3±51.9	0.417

Data presented as mean±standard deviation.

Discussion

The results of our study suggest that MRCP has a high predictive value in the diagnosis CBD obstruction and that while US alone has low predictive value, combined use of MRCP and US may further improve the diagnostic yield. On the other hand, despite their common use in the clinical practice, traditional of biochemical tests seemed to have no role in predicting a diagnosis of CBD. Also, patients over 50 years of age were significantly more likely to be diagnosed with obstruction. To our knowledge, this is one of the few studies comparing multiple diagnostic methods in CBD obstruction confirmed by ERCP.

MR cholangiopancreatography is justified as a routine preoperative imaging modality for cholecystectomy candidates with suspicious findings of obstruction on ultrasound, laboratory assessments, and clinical findings. Although endoscopic retrograde cholangiopancreatography is the main diagnostic and therapeutic intervention for the obstructed bile duct, it is also associated with major complications.

In our study, there was no difference between patients with and without biliary obstruction in terms of biochemical parameters and none of these parameters had predictive value for the diagnosis of obstruction. This finding is in line with previous studies concluding that liver test parameters cannot be considered an accurate predictor for common bile duct stones [8,9]. However, in patients with suspected CBD obstruction, biochemical parameters may be used as a guidance for further imaging methods. Despite some studies suggesting that elevated serum bilirubin and alkaline phosphates could represent better predictors of biliary obstruction as compared to liver enzymes [3,10], we failed to observe such a diagnostic value for these two parameters. On the other hand, in the study by Yu et al., the reported sensitivity and specificity of total bilirubin level, which was the most valuable biochemical parameter for CBD obstruction among six liver enzymes, was 55%, and 73%, respectively, for the prediction of CBD stones [8].

MRCP is not only a useful method to initially evaluate the abnormalities of common bile duct [8,11,12], but it is also a valuable tool to identify the etiology of common bile duct stones and to exclude further need for ERCP [3,10,12-17]. In addition, similar to our observations, this non-invasive technique compares more favorably to liver enzymes or ultrasound alone for the diagnosis of com-

mon bile duct obstruction [11,13]. In a study by Toppi et al. involving 201 patients, the specificity and sensitivity of MRCP in identifying CBD obstruction were 97%, and 98%, respectively; this is similar to the sensitivity rate, i.e. 95%, in our study [6]. On the other hand, in the Anand et al.'s study involving 224 patients considered to be high-risk for CBD (based on demographic, laboratory, and imaging findings), 168 patients underwent ERCP only, and 48 underwent both MRCP and ERCP, with no difference in the rate of diagnosis of CBD stones between the two groups [9]. As in our study, these authors also reported a high predictive value for MRCP. On the other hand, although MRCP was associated with high diagnostic yield in patients already scheduled for ERCP, it has also been emphasized that MRCP was not actually a necessary procedure [18]. In Anand et al.'s study, the authors pointed out to significant cost and workload savings by avoiding from MRCP in those 168 patients scheduled for an ERCP. Although ERCP is an invasive procedure associated with morbidities, its therapeutic potential should also be taken into account. Likewise, MRCP alone was associated with high diagnostic yield in our study, with further diagnostic contributions when US was added.

In our study, the remarkably high false negative rates associated with ultrasound alone (31.9%) as compared to MR (4.2%) indicate that almost one third of positive cases may be overlooked when US is used alone in this group of patients. Farrukh et al. recommended US only as an initial examination for obstruction to guide for further invasive and non-invasive methods (e.g. MRCP or ERCP) [25]. Also, in the study by Hajibandeh S. et al. [8] with 1022 patients, elevated liver enzymes or stones and related findings of dilation on US did not predict the presence of stones in the CBD. Also, Al-Jiffry et al. observed that the presence of stones in the common bile duct was reported preoperatively on US in only 57.2% of the patients who underwent exploration of the common bile duct and stone extirpation [13]. Similarly, US alone had a high false negative rate (31.9%) in determining dilation of the CBD in our study.

The main risk factors for cholesterol stone formation include female sex, pregnancy, high dose estrogen treatment, increasing age, genetic predisposition, obesity, and high serum triglyceride levels [1,3,9]. Population based studies showed a trend toward a higher risk of common bile duct obstruction with increasing mean age [3,8,13,19]. In line with these observations, our patients with biliary obstruction were significantly older, and older age had a high positive predictive value for obstruction.

This study has several limitations. Firstly, the gold standard diagnostic method, i.e. ERCP, was performed only if at least one of the other diagnostic procedures (laboratory, US, or MRCP) were suggestive of CBD. Thus, patients with no abnormalities in these three parameters were not included, since they did not undergo an ERCP. Other limitations include relatively small sample size and retrospective design.

Conclusion

MRCP, particularly when combined with ultrasound, is a useful diagnostic tool for the diagnosis of common biliary duct obstruction and may have the potential to eliminate the need for further ERCP in some patients. Further studies with prospective design and larger sample size are warranted to reach firm conclusions.

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Commento e Commentary

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L'articolo è relativo alla valutazione comparativa sull'efficacia e sensibilità diagnostica tra l'Ecografia e la Colangiopanreatografia RM, nella diagnosi di ostruzione biliare. Premesso che tale studio non può essere considerato innovativo, lo studio è stato condotto su un buon numero di pazienti, e i risultati ottenuti sono conformi a quelli della letteratura internazionale. Non si condivide la dichiarazione che la ERCP sia l'indagine diagnostica di prima scelta nella ostruzione della via biliare, infatti le Linee Guida della ESGE (European Society of Gastrointestinal Endoscopy), la considerano esclusivamente una indagine terapeutica da utilizzare dopo la positività diagnostica dell'ecografia e della Colangiografia RM, inoltre è stata introdotta in questo tipo di studio l'Ultrasonografia Endoscopica EUS, che ha una specificità e una sensibilità superiore all'ecografia addominale. Si auspica che in futuro lo studio venga condotto tra la Colangiopancreatografia RM e l'Ultrasonografia Endoscopica.

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The article is related to the comparative evaluation on the effectiveness and diagnostic sensitivity between ultrasound and MRI cholangiopanreatography, in the diagnosis of biliary obstruction. Given that this study cannot be considered innovative, the study was conducted on a good number of patients, and the results obtained are consistent with those of the international literature.
The claim that the ERCP is the first choice diagnostic investigation in the obstruction of the biliary tract is not shared, in fact the Guidelines of the ESGE (European Society of Gastrointestinal Endoscopy), consider it exclusively a therapeutic investigation to be used after the diagnostic positivity of the Echography and MRI Cholangiography, EUS Endoscopic Ultrasonography, which has a specificity and sensitivity superior to abdominal ultrasound, was also introduced in this type of study.
It is hoped that in the future the study will be conducted between MRI Cholangiopancreatography and Endoscopic Ultrasonography.