ENDOSCOPIC ULTRASOUND VERSUS ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY FOR THE DIAGNOSIS OF CHOLEDOCHOLITHIASIS: the influence of the size of the stone and diameter of the common bile duct*

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ABSTRACT – ***Background*** - Endoscopic retrograde cholangiography is highly accurate in diagnosing choledocholithiasis, but it is the most invasive of the available methods. Endoscopic ultrasonography is a very accurate test for the diagnosis of choledocholithiasis with a risk of complications similar to that of upper gastrointestinal endoscopy. ***Aim*** - To compare the accuracy of endoscopic ultrassonography and endoscopic retrograde cholangiography in the diagnosis of common bile duct stones before laparoscopic cholecystectomy and to analyze endoscopic ultrasound results according to stone size and common bile duct diameter. ***Patients and Methods*** - Two hundred and fifteen patients with symptomatic gallstones were admitted for laparoscopic cholecystectomy. Sixty-eight of them (31.7%) had a dilated common bile duct and/or hepatic biochemical parameter abnormalities. They were submitted to endoscopic ultrassonography and endoscopic retrograde cholangiography. Sphincterotomy and sweeping of the common bile duct were performed if endoscopic ultrassonography or endoscopic retrograde cholangiography were considered positive for choledocholithiasis. After sphincterotomy and common bile duct clearance the largest stone was retrieved for measurement. Endoscopic or surgical explorations of the common bile duct were considered the gold-standard methods for the diagnosis of choledocholithiasis. ***Results*** - All 68 patients were submitted to laparoscopic cholecystectomy with intraoperative cholangiography with confirmation of the presence of gallstones. Endoscopic ultrassonography was a more sensitivity test than endoscopic retrograde cholangiography (97% vs. 67%) for the detection of choledocholithiasis. When stones >4.0 mm were analyzed, endoscopic ultrassonography and endoscopic retrograde cholangiography presented similar results (96% vs. 90%). Neither the size of the stone nor the common bile duct diameter had influence on endoscopic ultrasonographic performance. ***Conclusions*** - For a group of patients with an intermediate or moderate risk with respect to the likelihood of having common bile duct stones, endoscopic ultrassonography is a better test for the diagnosis of choledocholithiasis when compared to endoscopic retrograde cholangiography mainly for small-sized calculi.

HEADINGS – Endosonography. Cholangiopancreatography, endoscopic retrograde. Choledochotilhiasis, diagnosis. Common bile duct.

INTRODUCTION

In western countries, choledocholithiasis is found in 8% to 18% of patients with symptomatic gallstones[8]. Once discovered, common bile duct (CBD) stones should be removed to prevent the development of acute cholangitis, pancreatitis, hepatic abscess and secondary biliary cirrhosis.

In the era of laparoscopic cholecystectomy (LC), when CBD stones are suspected or confirmed, endoscopic retrograde cholangiography (ERC) and sphincterotomy (ES) can be performed before surgery. Decision analysis has shown that laparoscopic management of the gallbladder and CBD stones is the most efficient and cost-effective approach[7]. However, laparoscopic removal of CBD stones is also less available than ERC with ES in most countries.

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ERC is highly accurate in diagnosing CBD stones, but it is the most invasive of the available methods. ERC also presents the highest complication rate when compared to transabdominal ultrasonography (US), helical computed tomography (CT scan), endoscopic ultrasound (EUS) and magnetic resonance cholangiography (MRC). For patients with gallstones, preoperative ERC should be reserved for those with a high level of suspicion of CBD stone disease as determined by clinical presentation, laboratory and echographic findings[4].

While patients with gallstones and a low level of probability of coexistent choledocholithiasis should be sent to LC without further testing, those patients with intermediate and moderate levels of suspicion of CBD stones should be offered noninvasive and highly accurate tests to confirm the presence of CBD stones.

MRC is recognized as a highly accurate and noninvasive test for the diagnosis of CBD stones. However, it is also known that the size of the stone has influence on MRC results especially when the diameter of the stone varies from 3 to 5 mm[16]. ERP can also produce false negative results especially when small stones in a dilated CBD are present.

EUS is a very accurate test for the diagnosis of choledocholithiasis with a risk of complications similar to that of upper gastrointestinal endoscopy. However, there are no data dealing with the influence of the size of the stone or the diameter of the CBD on the accuracy of EUS.

The aim of this study was to compare the accuracy of EUS and ERC in the diagnosis of CBD stones before LC and to analyze EUS results according to stone size and CBD diameter.

PATIENTS AND METHODS

This unicentric, prospective, comparative study was conducted from January 2000 through December 2001 after approval by the Federal University of Goias, "Hospital das Clínicas" Institutional Review Board.

Two hundred and fifteen patients with symptomatic gallstones were admitted for LC. One hundred and two of them (47.4%) presented normal blood tests and no direct or indirect echographic signs of CBD stones. They were referred to LC without further imaging tests. Forty-five patients (20.9%) were either jaundiced or had clinical signs of cholangitis, acute pancreatitis, or presented unequivocal evidence of CBD stones on US or CT scans. These patients were submitted to ERC with ES.

Sixty-eight patients (31.7%) (49 women, 19 men; mean age 57 years, range 18-83 years) had a dilated CBD (>7 mm on conventional ecography) and/or hepatic biochemical parameter abnormalities (AST >2x nl; elevated alkaline phosphatase). They were classified as intermediate or moderate risk with respect to the likelihood of having choledocholithiasis at the time of EUS/ERC[4]. They were enrolled in the study after providing written documentation of informed consent for both EUS and ERC with possible ES. Before their inclusion in the study, 22 (32.3%) of them had been submitted to CT scan and another 8 (11.8%) of them, to MRC. Both tests resulted in negatives for CBD stones.

EUS was performed using a 7.5/12 MHz mechanical radial scanning probe (GIF-UM20, Olympus America, Inc., Melville, NY) attached to a US processor (EUM-30). Stones were defined as mobile hyperechoic spots with an acoustic shadow. With the aid of calipers the largest stones were measured and recorded. With the echoendoscope positioned at the apex of the duodenal bulb, the diameter of the CBD was evaluated and recorded. The same operator, using a standard video duodenoscope performed ERC immediately after EUS, in the same room. Cholangiography was obtained by the selective cannulation of CBD and injection of a 1:1 diluted solution of contrast medium (Omnipaque, Nicomed, Inc., São Paulo, SP, Brazil). High-resolution fluoroscopy was employed and a standard filming sequence was obtained, including but not limited to a preliminary film, of the sequence immediately after selective CBD cannulation/injection and after opacification of the entire length of the extrahepatic biliary tree. Changing patient position and tilting the fluoroscopic table were employed whenever the operator could not define a filling defect as an air bubble or a stone. Extra filming sequences were obtained as deemed necessary by the operator in order to better record the presence or absence of CBD stones. The filming sequence was also evaluated by a senior radiologist blinded to the EUS/ERC operator's conclusions. The radiologist's conclusions were recorded immediately prior to the decision on whether to perform ES. When either the operator or the radiologist considered ERC findings suspicious for CBD stones, ERC was considered positive for choledocholithiasis. The operator had a large experience both in ERC and EUS with more than 3.000 and 1.000 procedures performed, respectively.

ES and sweeping of the CBD were performed if EUS or ERC were considered positive for CBD stones. The extraction of fragments or granules irrespective of their size was considered positive confirmation of diagnosed CBD stones. Whenever possible, after ES and CBD clearance the largest stone was retrieved for measurement.

ES was not indicated only when both tests proved to be negative for CBD stones. Regardless of ES, the patients were submitted to LC with routine intraoperative cholangiography (IOC) 48-72 hours after EUS/ERC. The surgeon was not blinded to the EUS/ERC results. The surgeon recorded the findings of LC and IOC (presence or absence of CBD stones) in all cases.

Endoscopic or surgical explorations of the CBD were considered the gold-standard methods for the diagnosis of CBD stones. If neither of them were performed, IOC and clinical follow-up were adopted as the alternative standards for comparison with the EUS/ERC results.

Any occurrence of pancreatitis, hemorrhage and perforation using previously described criteria[5] was recorded.

Statistical analysis

Categorical data were analyzed using Wald's test. A *P* value less than 0.05 was considered significant.

RESULTS

From 68 enrolled patients, 33 of them (47.1%) proved (through endoscopic or surgical exploration of the extrahepatic

biliary tree) to have CBD stones. The size of the stones and CBD diameters are listed in Table 1. The mean size of the detected stones was 5.8 mm (3.7-6.3 mm).

TABLE 1 – Stone size* (n = 33) and CBD diameter (n = 68)**

	Stone size (mm)				CBD diameter (mm)			
	≤4.0	4.1-8	8.1-12	>12	<4.0	4-7	7.1-12	>12
n(%)	13(39.4)	9(27.3)	7(21.2)	4(12.1)	4(5.9)	24(35.3)	24(35.3)	16(23.5)

* Stone size was determined by EUS in 32 patients and by surgical exploration of the CBD in one patient. Neither EUS nor ERC detected the calculus in this patient
** CBD diameter was determined by EUS in all cases

In 35 patients (52.9%) no CBD stones were found. After a mean follow-up period of 14 months (range 11-20 mo) no patients presented clinical, biochemical or radiological evidence of CBD retained stones.

All 68 patients were submitted to LC with IOC with confirmation of the presence of gallstones.

EUS and ERC detected choledocholithiasis in 32 and 22 patients, respectively (Table 2). There were no cases in which a CBD stone was correctly detected by ERC but missed by EUS. The only case missed by EUS was not identified by ERC either. That patient presented a 12 mm CBD and a 4,0 mm stone. A duodenal diverticulum was also present in this case.

TABLE 2 – EUS versus ERC in the diagnosis of choledocholithiasis

	EUS (%)	ERC (%)	*P*
Sensitivity [CI]*	97 [91-100]	67[51-85]	0.002
Specificity	100	100	0.950
Accuracy [CI]	98 [95-100]	84[62-90]	0.002
PPV	100	100	
NPV	97	75	

[CI]* - 95% confidence interval

Thirteen patients presented CBD stones sized 4.0 mm or less. EUS and ERC detected them in 12 and 2 patients, respectively (Table 3).

TABLE 3 – EUS versus ERC in the diagnosis of CBD stones ≤4.0 mm

	EUS (%)	ERC (%)	*P*
Sensitivity [CI]*	92 [91-100]	15[0-45]	0.001
Specificity	100	100	0.99
Accuracy [CI]	98 [95-100]	91[62-90]	0.02

[CI]* - 95% confidence interval

For stones larger than 4.0 mm, ERC was as accurate as EUS (Table 4).

TABLE 4 – EUS versus ERC in the diagnosis of CBD stones >4.0 mm

	EUS (%)	ERC (%)	*P*
Sensitivity [CI]*	96 [88-100]	90[82-100]	0.06
Specificity	100	100	0.99
Accuracy [CI]	98 [95-100]	92[86-100]	0.15

[CI]* - 95% confidence interval

The performance of EUS was analyzed according to subgroups of stone size and CBD diameters (Tables 5, 6).

TABLE 5 – Effect of size of CBD stones on EUS performance

	≤4.0 mm	>4.0 mm	*P*
Sensitivity [CI]*	92 [91-100]	96 [88-100]	0.35
Specificity	100	100	0.97
Accuracy[CI]*	98 [95-100]	98 [95-100]	0.32

[CI]* - 95% confidence interval

TABLE 6 – Effect of CBD diameter on the EUS performance

	≤7.0 mm	>7.0 mm	*P*
Sensitivity [CI]*	100 [91-100]	96 [88-100]	0.40
Specificity	100	100	0.98
Accuracy[CI]*	100 [95-100]	98 [95-100]	0.36

[CI]* - 95% confidence interval

Thirty-two patients were submitted to ES for stone extraction. Two of them (6.2%) developed mild pancreatitis. No patients presented bleeding or perforation caused by ES.

DISCUSSION

In centers where an ERC expert is available but advanced laparoscopic biliary tract surgery is not, the preoperative diagnosis of CBD stones becomes important in order to refer the patient to ES and endoscopic CBD clearance before LC. However, when CBD stones are suspected preoperatively based on clinical, biochemical tests and US indirect findings, a normal preoperative ERCP is still obtained in 40% to 70% of the patients with gallstones[11]. In the present study CBD stones were found in only 47.1% of a group of patients with abnormal biochemical tests and/or CBD dilation on US, meaning a 53.1% of "unnecessary" ERCs. Those data support the need for noninvasive, high-accuracy tests for the diagnosis of choledocholithiasis in order to limit the exposure of these patients to the added morbidity of ERC.

A limitation of the studies which assess the performance of a test for detection of choledocholithiasis is that ERC is generally used as the reference standard for the presence or absence of stones. It is well-recognized that small stones in a dilated CBD may be missed by ERC. In the present study, endoscopic or surgical exploration of the biliary tract was considered the gold standard. On the other hand, when both EUS and ERC resulted in a negative for CBD stones, it was felt unethical to perform ES just to validate the findings. For those cases a third test was performed, IOC. It seemed reasonable to consider a patient a true negative for choledocholithiasis if EUS, ERC and IOC proved negative for CBD stones and if/she remained asymptomatic 1 year after the LC.

There are nine studies which include a total of 601 patients comparing EUS and ERC to diagnose CBD stones[1, 2, 3, 6, 10, 12, 13, 14, 15]. In eight of these studies, endoscopic exploration of the CBD was used as the reference standard. All of these studies indicate that EUS and ERC have similar sensitivity and specificity in the detection of CBD stones. In the present study, ERC presented a rather low sensitivity (67%) in the diagnosis of choledocholithiasis when compared to other series. It must be pointed out that almost 40% of the patients presented stones smaller than 4.1 mm and almost 60% of them presented a dilated (>7.0 mm) CBD. Additionally, the mean size of the detected stones was 5.8 mm. The mean sizes in

other studies were usually higher: 6.9 mm[2] and 10.5 mm[12]. The association of small stones in a large duct could explain the low sensitivity of ERC. In fact, ERC and EUS had similar sensitivity when patients with stones larger than 4.0 mm were analyzed.

The present study has the potential for bias in the method for assessing the diagnostic performance of the tests because the same examiner performed both the EUS and the ERC. Bias was minimized by requiring a senior radiologist to document his interpretation of the ERC findings immediately before the clinical decision on performing ES.

SUGIYAMA et al.[16] did the only study that analyzed sensitivity of a test for CBD stone detection according to subgroups of stone size. Sensitivity of MRCP varied from 100% for 11-27 mm stone diameter to 71% for stones sized between 3-5 mm. Before their inclusion in the present study, eight patients (11.8%) had been submitted to MRCP with negative results. All of them presented CBC stones of 4.0 mm or less. EUS correctly diagnosed them in seven patients.

In the present study radial EUS was used for all examinations but similar performances were described when linear EUS was employed to detect CBD stones[9].

To the best of our knowledge this is the only study that has compared the diagnostic performance of EUS and ERC for choledocholithiasis according to stone size. Our results confirm the general impression that the diagnostic performance of EUS for CBD stone detection is not dependent either on stone size or on duct diameter.

It must be also emphasized that ES for CBD clearance was done immediately after EUS, in the same room, by the same operator, under the same sedation with obvious advantages for the patient and possibly being a rational approach from the cost standpoint. All these facts make the inclusion of EUS in the diagnostic algorithm of choledocholithiasis very attractive, especially for a group of patients with an intermediate or moderate risk with respect to the likelihood of having CBD stones.

Ney MVS, Maluf-Filho F, Sakai P, Zilberstein B, Gama-Rodrigues J, Rosa H. Ecoendoscopia versus colangiografia retrógrada endoscópica para o diagnóstico da coledocolitíase: a influência do tamanho do cálculo e do diâmetro da via biliar principal. Arq Gastroenterol 2005;42(4):239-43.

RESUMO - ***Racional*** - A colangiografia retrógrada endoscópica é método acurado porém invasivo para o diagnóstico da coledocolitíase. A ecoendoscopia também é método bastante eficaz para a detecção de cálculo coledociano e apresenta riscos semelhantes àqueles de uma endoscopia digestiva convencional. ***Objetivos*** - Comparar a acurácia da ecoendoscopia e da colangiografia endoscópica para o diagnóstico do cálculo da via biliar principal antes da colecistectomia laparoscópica e analisar a influência do tamanho do cálculo e do calibre da via biliar principal na eficácia diagnóstica da ecoendoscopia. ***Pacientes e Métodos*** - Duzentos e quinze pacientes com colecistolitíase sintomática foram admitidos para colecistectomia laparoscópica. Destes, 68 (31,7%) apresentaram dilatação da via biliar extra-hepática à ecografia convencional e/ou alteração de enzimas hepáticas e canaliculares. Foram, então, submetidos a ecoendoscopia e colangiografia endoscópica, seguida de papilotomia, se qualquer um dos métodos sugerisse a presença de coledocolitíase. Após a papilotomia, o maior cálculo foi recuperado e medido. A exploração endoscópica ou cirúrgica da via biliar foi considerada o padrão-ouro para o diagnóstico de coledocolitíase. ***Resultados*** - Todos os 68 pacientes foram submetidos a colecistectomia laparoscópica com colangiografia intra-operatória, comprovando-se colecistolitíase neste grupo. A ecoendoscopia foi mais sensível do que a colangiografia endoscópica para a detecção de cálculos coledocianos (97% vs. 67%). Para os cálculos maiores de 4,0 mm, os métodos apresentaram sensibilidades semelhantes (96% vs. 90%). Os resultados da ecoendoscopia não foram influenciados pelo tamanho do cálculo ou pelo calibre do colédoco. ***Conclusões*** - Para pacientes com risco intermediário para coledocolitíase, a ecoendoscopia é método mais sensível do que a colangiografia endoscópica, especialmente para cálculos pequenos.

DESCRITORES – Endossonografia. Pancreatocolangiografia retrógrada endoscópica. Coledocolitíase, diagnóstico. Ducto biliar comum.

REFERENCES

1. Burtin P, Palazzo L, Canard JM, Person B, Oberti F, Boyer J. Diagnostic strategies for extrahepatic cholestasis of indefinite origin: endoscopic ultrasonography or retrograde cholangiography? Results of a prospective study. Endoscopy 1997;29:349-55.
2. Canto MI, Chak A, Stellato T, Sivak MV Jr. Endoscopic ultrasonography versus cholangiography for the diagnosis of choledocholithiasis. Gastrointest Endosc 1998;47:439-48.
3. Chak A, Hawes RH, Cooper GS, Hoffman B, Catalano MF, Wong RC, Hevebener TE, Sivak MV Jr. Prospective assessment of the utility of EUS in the evaluation of gallstone pancreatitis. Gastrointest Endosc 1999;49:599-604.
4. Cohen S, Bacon BR, Berlin JA, Fleischer D, Hecht GA, Loehrer PJ Jr, McNair AE Jr, Mulholland M, Norton NJ, Rabeneck L, Ransohoff DF, Sonnenberg A, Vannier MW. National Institutes of Health State-of-the-Science Conference Statement: ERCP for diagnosis and therapy, January 14-16, 2002. Gastrointest Endosc 2002;56:803-9.
5. Cotton PB, Lehman G, Vennes J, Geenen JE, Russell RC, Meyers, Liguory C, Nickl N. Endoscopic sphincterotomy complications and their management: an attempt at consensus. Gastrointest Endosc 1991;37:383-93.
6. Dancygier H, Nattermann C. The role of endoscopic ultrasonography in biliary tract disease: obstructive jaundice. Endoscopy 1994;26:800-2.
7. Erickson RA, Carlson B. The role of endoscopic retrograde cholangiopancreatography in patients with laparoscopic cholecystectomies. Gastroenterology 1995;109:252-63.

8. Ko CW, Lee SP. Epidemiology and natural history of common bile duct stones and prediction of disease. Gastrointest Endosc 2002;56(6 Suppl):s165-s9.
9. Kohut M, Nowakowska-Dulawa E, Marek T, Kaczor R, Nowak A. Accuracy of linear endoscopic ultrasonography in the evaluation of patients with suspected common bile duct stones. Endoscopy 2002;34:299-303.
10. Norton SA, Alderson D. Prospective comparison of endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in the detection of bile duct stones. Br J Surg 1997;84:1366-9.
11. Petelin JB. Laparoscopic approach to common duct pathology. Am J Surg 1993;165:487-91.
12. Polkowski M, Palucki J, Regula J, Tilszer A, Butruk E. Helical computed tomographic cholangiography versus endosonography for suspected bile duct stones: a prospective blinded study in non-jaundiced patients. Gut 1999;45:744-9.
13. Prat F, Amouyal G, Amouyal P, Pelletier G, Fritsch J, Choury AD, Buffet C, Etienne JP. Prospective controlled study of endoscopic ultrasonography and endoscopic retrograde cholangiography in patients with suspected common-bile duct lithiasis. Lancet 1996;347:75-9.
14. Sugiyama M, Atomi Y. Endoscopic ultrasonography for diagnosing choledocholithiasis: a prospective comparative study with ultrasonography and computed tomography. Gastrointest Endosc 1997;45:143-6.
15. Sugiyama M, Atomi, Y. Acute biliary pancreatitis: the roles of endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography. Surgery 1998;124:14-21.
16. Sugiyama M, Atomi Y, Hachiya J. Magnetic resonance cholangiography using half-Fourier acquisition for diagnosing choledocholithiasis. Am J Gastroenterol 1998;93:1886-90.

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