Triple non-invasive diagnostic test for exclusion of common bile ducts stones before laparoscopic cholecystectomy

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Received: July 10, 2007 Revised: August 17, 2007

Abstract

AIM: To evaluate the impact of a preoperative "triple non-invasive diagnostic test" for diagnosis and/or exclusion of common bile duct stones.

METHODS: All patients with symptomatic gallstone disease, operated on by laparoscopic cholecystectomy from March 2004 to March 2006 were studied retrospectively. Two hundred patients were included and reviewed by using a triple diagnostic test including: patient's medical history, routine liver function tests and routine ultrasonography. All patients were followed up 2-24 mo after surgery to evaluate the impact of triple diagnostic test.

RESULTS: Twenty-five patients were identified to have common bile duct stones. Lack of history of stones, negative laboratory tests and normal ultrasonography alone was proven to exclude common bile duct stones in some patients. However, a combination of these three components (triple diagnostic), was proven to be the most statistically significant test to exclude common bile duct stones in patients with gallstone disease.

CONCLUSION: Using a combination of routinely used diagnostic components as triple diagnostic modality would increase the diagnostic accuracy of common bile duct stones preoperatively. This triple non-invasive test is recommended for excluding common bile duct stones and to identify patients in need for other investigations.

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Key words: Common bile duct stones; Laparoscopic cholecystectomy; Triple non-invasive diagnostic test

Pourseidi B, Khorram-Manesh A. Triple non-invasive diagnostic test for exclusion of common bile ducts stones

before laparoscopic cholecystectomy. *World J Gastroenterol* 2007; 13(43): 5745-5749

<http://www.wjgnet.com/1007-9327/13/5745.asp>

INTRODUCTION

Surgery is the treatment of choice in symptomatic gallstone disease and is also recommended in asymptomatic patients due to complications followed by stone release in common bile duct^[1-5]. Coexisting common bile duct stones (CBDS) occur in 7%-20% of all patients undergoing cholecystectomy^[2,3,6]. Although intraoperative cholangiography was routinely performed to diagnose CBDS during pre-laparoscopic era, its use in the laparoscopic era has been debated^[7-10]. Consequently, other techniques for diagnosing CBDS have been introduced^[6-8].

Preoperative liver function test (LFT) results might be diagnostic for CBDS, if abnormal. However, some patients might have normal LFT despite coexisting CBDS^[5,7]. Ultrasonography is the major diagnostic modality to diagnose gallstones, but is less helpful for diagnosing CBDS^[1-7]. Computed tomography is rarely useful for diagnosing gallstones^[5,8]. Magnetic-resonance-cholangio-pancreatography (MRCP) has high specificity and sensitivity and accuracy similar to that of Endoscopic-Retrograde-Cholangio-Pancreatography (ERCP), but its accuracy decreases if gallstones are small (< 4 mm) or if they are located near Vater's papilla^[2,5,8,11]. In addition, MRCP is not widely available and unlike ERCP does not allow endoscopic extraction of stones^[5,8,12]. ERCP is the most common technique used for both diagnostic and treatment of CBDS. It is however, expensive, invasive, technically demanding and associated with small but significant morbidity^[6,7,13].

Clinical history of jaundice, pancreatitis or cholangitis, abnormal LFT results and or dilated common bile duct have been traditionally used to select possible candidates for ERCP preoperatively^[5], but to the best of our knowledge, the accuracy of these parameters together in diagnosing and/or excluding CBDS has never been evaluated^[5,6,8]. The aim of this retrospective study was to assess the accuracy of these variables alone and in combination for diagnosing/excluding CBDS in a consecutive group of patients with symptomatic gallstones disease operated on by laparoscopic cholecystectomy.

MATERIALS AND METHODS

From March 2004 to March 2006, all consecutive patients with ultrasound verified gallstones, in whom laparoscopic cholecystectomy was indicated, were studied retrospectively. The study was approved by the Afzali Hospital's ethical committee.

All information was collected based on a questionnaire including three different components. Patient's data and medical history, age at operation, gender, history of jaundice (obstructive *vs* non-obstructive), cholangitis or pancreatitis (acute *vs* non-acute) were recorded. The results of ultrasonography, preoperative liver functions tests (LFT), serum-total bilirubin (S-Bil), alkaline phosphatase (S-ALP) and white blood cells counts (WBC) were obtained. The following cut-off values were considered abnormal: S-Bil ≥ 1.5 dL/L, S-ALP ≥ 400 UI/L and WBC $\geq 10\,000/\text{mm}^3$. CBDS diagnosis was established by either demonstrating a stone in CBD or a wide CBD (diameter ≥ 10 mm). All patients were operated laparoscopically. No intraoperative cholangiography was performed. All included patients ($n = 200$) were followed up 2-24 mo postoperatively, by means of a questionnaire, completed by telephone interviews or clinical visit if needed.

Statistical analysis

The statistical analysis was performed using SPSS (version 11.0). The association between occurrence of CBDS and different variables was analyzed using Chi-square test. Sensitivity, specificity, positive and negative predictive values were calculated for all variables individually and in combination. Student *t*-test with separate variance estimates was performed to test the demographic differences. Fisher exact test and χ^2 -test were performed to compare between patients with a different number of suggested variables. $P < 0.05$ was considered statistically significant. Any patient with incomplete medical file or test results or any unclear information was excluded.

RESULTS

Two hundred patients, 43 men (21.5%) and 157 women (78.5%) were consecutively included in this study. The mean age of patients at the time of operation was 56.6 ± 18.2 and 51.6 ± 16.5 years for men and women, respectively. The average length of hospital stay was 30 (range 24-72) h for the whole group of patients, with no statistically significant difference between men and women.

Eighteen patients (9%) were found to have CBDS intraoperatively and additional 7 patients were found to have CBDS during the follow-up. The total number of patients with CBDS in this series was 25 patients (12.5%). The review of patient's clinical history did not reveal any clinical evidence for CBDS (jaundice, cholangitis or pancreatitis) in the majority of patients (89.5%). In the remaining patients (10.5%), besides cholangitis, all other clinical variables were more common in men. In 16 out of 25 patients with CBDS (8 women and 8 men), obstructive jaundice was the most frequent variable in both genders (Table 1). The association between clinical evidence for

Table 1 Frequency of clinical variables in 200 patients with gallstones n (%)

Variables	Total	Women	Men
Obstructive jaundice			
Yes	16 (8)	8 (5.1)	8 (18.6)
No	183 (92)	148 (94.9)	35 (81.4)
Total	199 (100)	156 (100)	43 (100)
History of jaundice			
Yes	5 (2.5)	3 (1.9)	2 (4.7)
No	192 (97.5)	151 (98.1)	41 (95.3)
Total	197 (100)	154 (100)	43 (100)
Cholangitis			
Yes	5 (2.5)	5 (3.2)	0
No	192 (97.5)	149 (96.8)	43 (100)
Total	197 (100)	154 (100)	43 (100)
Acute Pancreatitis			
Yes	1 (0.5)	0	1 (2.3)
No	196 (99.5)	154 (100)	42 (97.7)
Total	197 (100)	154 (100)	43 (100)
History of Pancreatitis			
Yes	2(1)	1 (0.6)	1 (2.3)
No	195(99)	153 (99.4)	42 (97.7)
Total	197(100)	154 (100)	43 (100)

Table 2 Association between the number of positive clinical variables and CBDS n (%)

Patients	Negative history	1 positive findings	2 positive findings	Total
Men	34 (79.1)	6 (14)	3 (7)	43 (100)
Women	145 (92.4)	7 (4.5)	5 (3.2)	157 (100)
Total	179 (89.5)	13 (6.5)	8 (4)	200 (100)

CBDS and occurrence of CBDS was calculated (Table 2). Thirteen patients had one positive clinical variable and 8 patients had two positive clinical variables. Higher number of positive clinical variables was not statistically significant for diagnosing CBDS. CBDS was more common in men with clinical evidence of the disease. The difference between men and women in this aspect was statistically significant (Chi-square: 6.56, df: 2, $P < 0.05$) (Table 2).

The majority of patients in this cohort had a normal ultrasonography ($n = 175$, 87.3%). However, in 25 patients with CBDS (12 women and 13 men), 8 patients had a stone in common bile duct, 12 had obstruction in common bile duct, one had both a stone and obstruction of common bile duct, 3 had a widened common bile duct (> 10 mm), and finally one patient had widening of an intrahepatic bile branch. Positive ultrasonographic findings indicating CBDS were more common in men [13 out of 43 men (30%) and 12 out of 157 women (7%)] (Table 3). The difference in ultrasonographic diagnosis between men and women was statistically significant (Chi-square 20.23, df: 5 and $P < 0.05$).

The abnormal S-Bil and S-ALP results in men and women with CBDS are shown in Table 4. The majority of patients had normal laboratory results ($> 85\%$). In 13 men (30.2%) serum bilirubin concentration was higher than 1.5 dL/L [compared to 11 women (7%)] and in 14 men (32.6%) the concentration of alkaline phosphatase was higher than 400 UI/L [compared to 16 women (10%)]. All

Table 3 The results of ultrasound investigations in 200 patients with gallstones (per gender) *n* (%)

Patients	Men	Women	Total
CBDS	5 (11.9)	3 (1.9)	8 (4.1)
CBD obstruction	6 (14.3)	6 (3.9)	12 (6.1)
CBDS and obstruction	1 (2.4)	0 (0)	1 (0.5)
CBD diameter > 10 mm	1 (2.4)	2 (1.3)	3 (1.5)
Dilated intrahepatic bile duct branches	0 (0)	1 (0.6)	1 (0.5)
Normal	30 (69)	145 (92.3)	175 (87.3)
Total	43 (100)	157 (100)	200 (100)

CBD: Common bile duct; CBDS: Common bile duct stones.

Table 4 Results of liver tests in patients with gallstones (per gender) *n* (%)

Gender	S-bilirubin ≥ 1.5 dL/L			Alkaline phosphatase ≥ 400 U/L		
	Yes	No	Total	Yes	No	Total
Men	13 (30.2)	30 (69.8)	43 (100)	14 (32.6)	29 (67.4)	43 (100)
Women	11 (7)	146 (93)	157 (100)	16 (10.2)	141 (89.8)	157 (100)
Total	24 (12)	176 (88)	200 (100)	30 (15)	170 (85)	200 (100)

patients with S-Bil ≥ 1.5 dL/L had CBDS. These changes were more common in men and the difference between men and women was statistically significant (Chi-square 17.24, df: 1 and $P < 0.05$).

The sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) of each variable of medical history, LFT results and ultrasonography alone or in different combination for diagnosis/exclusion of CBDS was evaluated statistically (Table 5). As a single diagnostic test, ultrasonography had higher sensitivity (64%), specificity (97.1%), negative and positive predictive values (95% and 76.2%, respectively) than medical history, S-Bil and S-ALP. As a triple diagnostic modality, a combination of medical history, ultrasonographic findings and LFT results was proven to be the best diagnostic modality to exclude CBDS. White blood cells count had no impact in diagnosis of CBDS.

DISCUSSION

Although the majority of patients with gallstone disease have an uncomplicated surgical course, a few may become complicated due to occurrence of CBDS^[1-3]. Due to fewer intraoperative cholangiographies during laparoscopic cholecystectomies^[6,7], ERCP has been recommended for pre- or postoperative extraction of CBDS. It is however, an invasive investigation with high risk for complications and should be reserved for selected cases^[12,14,15]. MRCP is not available in all institutions and its accuracy depends on the size and position of CBDS^[4,11,12]. There is thus a need for easy-performing, non-invasive, and reliable test modalities to diagnose or exclude CBDS, by which selected patients can benefit from ERCP, MRCP or other expensive investigations^[13-15]. Earlier studies on some clinical, laboratory or radiological variables have been performed^[16,17]. There is however, as far as we know,

Table 5 Diagnostic value of each of the triple tests, alone and in combination *n* (%)

Variables	Sensitivity	Specificity	NPV	PPV
1. Medical history	44	92.5	90.5	38.1
2. Ultrasound	64	97.1	95	76.2
3. Alkaline phosphatase ≥ 400 U/L	32	95	90	26.7
4. Serum bilirubin ≥ 1.5 dL/L	30.3	76.2	89.2	25
2 + 3 + 4	80	82.9	96.7	40
2 + 3 or 2 + 4	32	97.1	90.9	61.5
2 + 1 + 3 or 4	84	81.7	97.3	39.6

NPV: Negative predictive value; PPV: Positive predictive value.

no study performed evaluating a combination of these investigating modalities. The majority of patients with gallstones are routinely evaluated by their clinical history, ultrasonography and LFT (S-Bil and S-ALP)^[3,5]. The main object of this study was to evaluate the efficacy of these non-invasive investigation methods for exclusion of CBDS diagnosis.

The importance of careful review of patient's history has been reported in many earlier studies. A focused positive patient's history may be an early indication of CBDS^[3,6,16-18]. Hyperbilirubinemia preoperatively, had a high diagnostic significant in our study and is also reported by others^[7,19]. Ultrasonographic investigation is a reliable diagnostic modality with high availability and lower cost. However, the result of the investigation depends highly on investigators experience^[3,14,20]. In our study, ultrasonography was performed by one radiologist and our results are comparable with earlier reports^[3,6]. As also earlier reported by others, our study indicates that in patients who lacked clinical, radiological and laboratory signs of CBDS, there is no need for performing ERCP^[6,14,21-25]. It also indicates that by using patient's complete medical history (with special focus on the most common clinical complication of gallstone diseases such as pancreatitis), customary laboratory tests such as S-Bil and S-ALP and ultrasonography one may exclude CBDS diagnosis with high accuracy^[26-29].

We used different variables as predictors *i.e.*, these variables were used to predict or explain the value(s) of one or more dependent variables (also referred to as dependent or outcome variables statistically). The positive predictive value (PPV), or precision rate, is defined as the proportion of patients with positive test results who are correctly diagnosed. Hence the PPV is used to indicate the probability that, in case of a positive test, the patient really has the specified disease. However there may be more than one cause for a disease and any single potential cause may not always result in the overt disease seen in a patient. In our study only ultrasonographic investigation has highest PPV followed by a combination of ultrasound investigation and LFT results. Since we were interested in evaluating the impact and usefulness of the negative ultrasonography or LFT results and the lack of clinical evidence (negative history of pancreatitis, cholecystitis and cholangitis) of CBDS, in our study, we used the negative predictive value (NPV), which is the proportion of patients with negative test results who are correctly

diagnosed. Higher NPV means then higher sensitivity for excluding CBDS as shown in our study; combining several tests in our study increased the negative predictive value and sensitivity of CBDS exclusion with almost equal specificity^[16-18,30].

We concluded that patients with normal ultrasonography, LFT results and no clinical evidence of CBDS “negative triple test” (NPV of 97.3%) may undergo laparoscopic surgery without any need for preoperative MRCP or ERCP. The availability and non-invasiveness of this triple diagnostic test are additional benefits, which makes it more interesting.

COMMENTS

Background

Coexisting common bile duct stones (CBDS) may complicate the course of gallstone disease. During open surgical removal of gallstones (open cholecystectomy), cholangiography is performed to exclude, or if needed, to remove CBDS. With laparoscopic cholecystectomy becoming the first surgical choice for treatment of gallstones, preoperative cholangiography has not been performed routinely and the procedure itself has been debated. Consequently, other techniques have been used to exclude CBDS. These techniques, however, are either invasive, with consequent risk for complications, or only diagnostic; some of them not available at all hospitals. There is thus a need to establish a simple, non-invasive and cheap diagnostic method, available at all units, to identify patients with CBDS for further evaluation with invasive and more expensive techniques.

Research frontiers

The research front in this area is focused on developing different imaging techniques. The most promising technique is Magnetic-Resonance-Cholangio-Pancreatography (MRCP). It has high specificity and sensitivity and accuracy similar to that of ERCP (Endoscopic-Retrograde-Cholangio-Pancreatography), but its accuracy decreases if gallstones are small (< 4 mm) or if they are located near Vater's papilla. In addition MRCP is not widely available and unlike ERCP does not allow endoscopic extraction of stones. ERCP is the most common technique used for both diagnostic and treatment of CBDS. It is however, expensive, invasive, technically demanding and associated with small but significant morbidity.

Innovations and breakthroughs

By using already existed parameters; liver functions test, ultrasonography together with complete review of patient's medical history (triple diagnostic), we offer a simple, cheap and, for all clinicians, available triple technique, to diagnose or exclude CBDS without any extra cost or diagnostic delay.

Applications

The majority of patients without CBDS will be identified by this triple diagnostic technique, leaving the remaining few, to be investigated by MRCP or ERCP. The availability and non-invasiveness of this test are additional benefits, which makes it more interesting.

Terminology

Cholangiography: X-ray examination of the bile ducts following administration of a radiopaque contrast medium. Magnetic-Resonance-Cholangio-Pancreatography: is a medical imaging technique which uses magnetic resonance imaging to visualise the biliary and pancreatic ducts in a non-invasive manner. Endoscopic-Retrograde-Cholangio-Pancreatography: refers to the use of an endoscope; a thin, flexible tube with a tiny video camera and light on the end to diagnose and treat various problems of the GI tract (stomach, intestine, liver, pancreas, and gallbladder).

Peer review

Through retrospective study, the authors concluded that using a combination of routinely used diagnostic components as triple diagnostic modality would increase the diagnostic accuracy of common bile duct stones. The result is reasonable and persuasive.

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