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Intraoperative cholangiography versus magnetic resonance cholangiography in patients with mild acute biliary pancreatitis

A prospective study in a second-level hospital

Gustavo Angel Gómez-Torres, MD^{a,*}, Jaime González-Hernández, MD^b, Carlos Rene López-Lizárraga, MD^c, Eliseo Navarro-Muñiz, MD^d, Odeth Sherlyne Ortega-García, MD^e, Francisco Manuel Bonnet-Lemus, MD^f, Francisco Manuel Abarca-Rendon, MD⁹, Liliana Faviola De la Cerda-Trujillo, PharmD^h

Abstract

Cholecystectomy is the only definitive management of pancreatitis secondary to gallstone disease. Approximately 20% to 30% of patients with acute biliary pancreatitis (ABP) will have persistent common bile duct (CBD) stones. Therefore, choosing a method for the early diagnosis of choledocholithiasis is essential to reduce waiting days for surgery and hospital stay in these patients.

The aim of this study was to compare the use of magnetic resonance cholangiography (MRC) and intraoperative cholangiography (IOC), and its impact on the length of the hospital stay in patients with mild ABP and an intermediate probability of choledocholithiasis.

We prospectively evaluated all patients diagnosed with mild ABP and an intermediate probability of choledocholithiasis at admission and 48 hours after, from June, 2017 to December, 2017. Study subjects were identified upon admission and were classified into 2 groups of patients according to their choledocholithiasis predictors; a MRC was performed in the group 1, and an IOC was done in group 2.

In all, 47 patients were enrolled in the final analysis of this study. Hospital stay in group 1 (CMR) patients was 8.29 (\pm 2.69) days compared with 6.43 (\pm 2.57) days in the group 2 (IOC) (P=.007). Mean waiting days for cholecystectomy was 17.14 (\pm 26.04) days for group 1 and 5 (\pm 2.69) days for group 2.

We suggest an IOC as the election method for the diagnosis of CBD stones in patients with mild ABP in medical centers similar to ours because it reduces waiting days for surgery and hospital stay compared to the MRC.

Abbreviations: ABP = acute biliary pancreatitis, ASGE = American Society for Gastrointestinal Endoscopy, CBD = common bile duct, ERCP = endoscopic retrograde cholangiopancreatography, EUS = endoscopic ultrasound, IOC = intraoperative cholangiography, MRC = magnetic resonance cholangiography.

Keywords: acute biliary pancreatitis, choledocholithiasis, intraoperative cholangiography, magnetic resonance cholangiography, probability of choledocholithiasis

1. Introduction

Acute pancreatitis is defined as the acute inflammatory condition of the pancreas secondary to early activation of digestive enzymes found inside the acinar cells.^[11] The gallstone disease is the most frequent etiology of acute pancreatitis representing 30% to 50%.^[2–4] Acute biliary pancreatitis (ABP) results from the

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^a Department of Colorectal Surgery, ^b Department of General Surgery, ^c Division of Surgery, ^d Department of General Surgery, ^e Department of Pediatrics,

^f Department of General Surgery, ^g Department of Colorectal Surgery,

^h Department of General Surgery, Hospital Civil de Guadalajara "Dr. Juan I. Menchaca", Guadalajara, Jalisco, Mexico.

^{*} Correspondence: Gustavo Angel Gómez-Torres, Department of Colorectal Surgery, Hospital Civil de Guadalajara "Dr. Juan I. Menchaca", Salvador Quevedo y Zubieta street #750, Guadalajara, Jalisco, Mexico (e-mail: gustavo_angel57@hotmail.com).

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Received: 30 June 2018 / Accepted: 2 October 2018 http://dx.doi.org/10.1097/MD.000000000012976 migration of a gallstone to the common bile duct (CBD), most of these gallstones are smaller than 5 mm in diameter.^[3,5–8] Although spontaneous passage of the CBD small stones occurs in up to 50% of the cases, 20% to 30% of patients with ABP will have persistent CBD stones.^[6,9–11] Thus, it is mandatory to image the CBD during inpatient admission to ensure the absence of choledocholithiasis.^[2,8]

The American Society for Gastrointestinal Endoscopy (ASGE) defines the ABP as a moderate predictor of choledocholithiasis, which means that a patient with this pathology has at least an intermediate probability of having a CBD stone (10%-50%). Options for evaluation of these group of patients include endoscopic ultrasound (EUS), magnetic resonance cholangiography (MRC), laparoscopic ultrasound, and intraoperative cholangiography (IOC).^[12]

Cholecystectomy is the only definitive management of pancreatitis secondary to gallstone disease, and it is advised to be performed within the same index admission.^[2,4,13–15] Therefore, choosing a method for the early diagnosis of choledocholithiasis is essential to reduce waiting days for surgery and hospital stay in patients with mild ABP.

The aim of this study was to compare the use of MRC and IOC in a second-level hospital, and its impact on the length of waiting days for surgery and the hospital stay in patients with mild ABP and an intermediate probability of choledocholithiasis.

The authors declare that they have no conflict of interests.

2. Patients and methods

The ethics committee of our medical center approved this study, and it was conducted in accordance with the ethical guidelines of the Declaration of Helsinki. Informed consent was obtained from all participants.

We prospectively evaluated all patients diagnosed with mild ABP and an intermediate probability of choledocholithiasis at admission and 48 hours after, from June, 2017 to December, 2017. The diagnosis of mild acute pancreatitis was based on the Atlanta guidelines,^[13] and the probability of choledocholithiasis was calculated according to the ASGE guidelines.^[12] Study subjects were identified upon admission by the general surgery service and were classified into 3 types of patients according to their choledocholithiasis predictors at the admission and 48 hours after (Fig. 1)—type 1: patients with a common bile duct >6mm; type 2: patients with high levels of alkaline phosphatase (ALP) or/and gamma-glutamyltransferase (GGT) after 48 hours admission and a common bile duct <6 mm; type 3: patients with normal levels of ALP and GGT after 48 hours admission and a common bile duct < 6 mm. A MRC was performed in type 1 and 2 patients (group 1), and an IOC was done in type 3 patients (group 2).

The inclusion criteria were age between 18 and 60 years, diagnosis of mild ABP according to Atlanta 2012 guidelines, an intermediate probability of choledocholithiasis 48 hours after admission. The exclusion criteria included a high probability of choledocholithiasis persisting 48 hours after admission, moderate or severe pancreatitis, renal or hepatic chronic disease, pregnancy, allergy to contrast medium, and patients who did not sign the consent form for the study. The characteristics of the patients in the groups were compared with the use of Student *t* test or Mann–Whitney *U* test depending on the distribution of continuous variables as appropriate, and Fisher exact test for categorical variables. We calculated the sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios of the ASGE individual predictors. The XLSTAT 19.7.4 statistical software package was used for the statistical analysis.

3. Results

In all, 71 patients were diagnosed with mild pancreatitis from June, 2017 to December, 2017. Seventeen patients were classified with a high probability of choledocholithiasis at admission without decreasing to intermediate probability after 48 hours, and 7 patients were pregnant during the APB episode. In all, 47 patients were enrolled in the final analysis of this study. The mean cohort age was 30.6 years (± 10.6), and 41 (87%) were female patients. Eleven (23.4%) of the patients were classified as type 1, 13 (27.6%) as type 2, and 23 (48.9%) patients as type 3. The characteristics of the 3 types of patients are shown in Table 1.

Magnetic resonance cholangiography was performed in 24 (51%) patients; 20 (83%) of the patients were female with a mean age of 32 (\pm 11.2). The diagnosis of choledocholithiasis was confirmed in 2 (8%) of the patients in this group. The IOC group included 23 patients; 21 (91%) of them were female with a mean age of 32.5 (\pm 10.2) years; choledocholithiasis was diagnosed in 1 (4.3%) patient.

The waiting time for the MRC group was of $4.9 (\pm 1.47)$ days and of 5 (± 2.69) days for the IOC group, and there was no



Figure 1. Classification of the type of patients. Type 1: intermediate probability of choledocholithiasis with CBD >6 mm. Type 2: intermediate probability of choledocholithiasis with CBD <6 mm with elevation GGT or ALP 48 hours after admission. Type 3: intermediate probability of choledocholithiasis with CBD <6 mm with normal GGT or ALP 48 hours after admission. MRC was performed in type 1 and 2 patients (group 1); IOC was done in type 3 patients (group 2). ALP = alkaline phosphatase, CBD = common bile duct, GGT = gamma-glutamyltransferase.

Table 1

Characteristics of the type of patients.

	Туре 1	Type 2	Туре 3
Patients	11	13	23
Female sex, no. (%)	9 (82%)	11 (85%)	21 (91%)
Male sex, no (%)	2 (18%)	2 (15%)	2 (9%)
Age, y	29.25 (±9.9)	34 (±12.5)	32.56 (±10.2)
Common bile duct, mm	8.2 (±1.8)	5.2 (±0.9)	4.37 (±1.12)
Total bilirrubin at admission, mg/dL	1.6 (±1.2)	4.06 (±2.3)	2.5 (±1.7)
Decrease of total bilirrubin, % mg/dL	37.12 (±17.05)	59.6 (±21.91)	44.41 (<u>+</u> 33.04)
GGT admission, UI/L	198 (±134.4)	430 (±264)	200.56 (±185.22)
ALP admission, U/L	160.9 (±97.81)	239 (±100)	152.13 (±55.77)
High probability of choledocholithiasis admission, no. %	4 (36%)	6 (46%)	5 (21.7%)
Choledocholithiasis, no. %	1 (9%)	1 (7%)	1 (4.3%)
Waiting days for MRC or IOC, d	4.8 (<u>+</u> 1.4)	5 (<u>+</u> 1.5)	5 (<u>+</u> 2.69)
Waiting days for surgery, d	27.4 (<u>+</u> 35.6)	7.8 (<u>+</u> 3.8)	5 (<u>+</u> 2.69)
Hospital stay, d	7.6 (<u>+</u> 1.28)	8.8 (<u>+</u> 3.4)	6.4 (<u>+</u> 2.5)

Means SD (±).

Type 1 = intermediate probability of choledocholithiasis with CBD > 6 mm. Type 2 = intermediate probability of choledocholithiasis with CBD < 6 mm with elevation GGT or ALP 48 hours after admission. Type 3 = intermediate probability of choledocholithiasis with CBD < 6 mm with normal GGT or ALP 48 hours after admission.

ALP = alkaline phosphatase, CBD = common bile duct, GGT = gamma-glutamyltransferase, IOC = intraoperative cholangiography, MRC = magnetic resonance cholangiography.

statistically significant difference between the 2 groups (P=.25). Mean waiting days for cholecystectomy were 17.14 (±26.04) days for group 1 (CRM) and 5 (±2.69) days for group 2 (IOC), with a statistical significance (P=.001) $\alpha=0.05$. It is important to mention that 3 of the patients in the MRC group were discharged before surgery, which was performed in a second admission. Hospital stay in group 1 patients was 8.29 (±2.69) days compared with 6.43 (±2.57) days in the group 2 (P=.007). The statistical analysis of the characteristics between the 2 groups is shown in Table 2.

We assessed the diagnostic performance of individual predictors for choledocholithiasis according to ASGE guidelines (Table 3). A common bile duct >6 mm showed a sensitivity of 33% and a specificity of 77%, with a positive predictive value (PPV) of 9% and negative predictive value (NPV) of 94%. Total

Table 2	
Statistical	differences between the groups.

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	Group 1 CMR	Group 2 IOC	Р					
Patients	24	23						
Female sex, no. (%)	20 (83%)	21 (91%)	.19					
Male sex, no (%)	4 (17%)	2 (9%)	.19					
Age, y	32 (±11.2)	32.5 (±10.2)	.7					
Common bile duct, mm	6.57 (± 2.0)	4.37 (±1.12)	.001					
Total bilirrubin at admission, mg/dL	2.96 (± 2.21)	2.5 (<u>+</u> 1.78)	.67					
Decrease of total bilirrubin, % mg/dL	52.12 (± 25.52)	44.41 (<u>+</u> 33.04)	.72					
GGT admission	318.25 (±239.3)	200.56 (±185.22)	.04					
ALP admission	203.66 (±239.3)	152.13 (<u>+</u> 55.77)	.11					
High probability of choledocholithiasis Admission, no. %	10 (41%)	5 (21%)	.4					
Choledocholithiasis, no. % Waiting days for MRC or IOC, d Waiting days for surgery, d Hospital stay, d	2 (8%) 4.9 (±1.47) 17.14 (±26.04) 8.29 (±2.69)	1 (4%) 5 (±2.69) 5 (±2.69) 6.43 (±2.57)	.16 .25 .001 .007					

Means SD (\pm); statistically significant (P<.05).

ALP = alkaline phosphatase, CBD = common bile duct, GGT = gamma-glutamyltransferase, IOC = intraoperative cholangiography, MRC = magnetic resonance cholangiography.

bilirubin at admission >1.8 mg/dL presented a sensitivity of 67% and a specificity of 36% (PPV of 7%, NPV of 95%).

To date, none of the patients included in our study has been readmitted for residual choledocholithiasis or a recurrence of ABP.

4. Discussion

The appropriate time for definitive treatment for patients with mild ABP has not yet been established, but the current recommendation is to perform a cholecystectomy during the initial hospitalization to prevent recurrence and readmission that may occur up to 31% in the first 2 weeks.^[3,16] The International Association of Pancreatology and the American Gastroenterological Association recommends that all patients with gallstone pancreatitis should undergo cholecystectomy as soon as the patient has recovered from the symptoms.^[17,18] Though, the most appropriate method for studying choledocholithiasis and the timing to evaluate the probability of common bile duct stone in the patients with ABP has not yet been established.

In clinical practice, the decision to perform IOC, MRC, EUS, laparoscopic ultrasound, or endoscopic retrograde cholangiopancreatography (ERCP) is often based on biological and radiological criteria; and depends on the resources and availability of diagnostic methods of the medical center.

To improve the approach in patients with risk of choledocholithiasis, the predictors proposed by the ASGE have been widely studied: among them are CBD >6 mm with a sensitivity 64.7% to 90% and specificity 23% to 76.1%, total bilirubin between 1.8 and 4 mg/dL, with sensitivity 19% to 61% and specificity 44% to 85%.^[19–22]. We found similar values for the sensitivity and specificity in the strong predictors. But the frequency of choledocholithiasis in patients with mild ABP, and intermediate probability for choledocholithiasis was smaller than the one referenced in the ASGE guidelines, with a 10% to 50% of probability, and the 23.5% reported for Narvaes-Rivera and cols in a Mexican population study.^[19]

The methods that we used for the diagnosis of choledocholithiasis were the IOC and the MRC. Recent studies have demonstrated MRC is an effective method to detect choledocholithiasis in patients with ABP, presenting a sensitivity of Table 3

Predictors	Sensitivity	Specificity	PPV	NPV	+LR	-LR
CBD >6 mm	0.33	0.77	0.09	0.94	1.47	0.86
Total bilirubin >1.8 mg/dl	0.67	0.36	0.07	0.95	1.05	0.91
GGT >62iU/L	1	0.11	0.07	1	1.13	0
ALP >126 U/L	1	0.32	0.09	1	1.47	0
High probability of choledocholithiasis	0.67	0.70	0.13	0.97	2.26	0.47

High probability of choledocholithiasis: subjects with the presence of any very strong predictor (CBD stone on abdominal US or clinical ascending cholangitis or bilirubin >4 mg/dL) or both strong predictors (bilirubin level 1.8-4 mg/dL + CBD > 6 mm).

+LR=positive likelihood ratio, -LR=negative likelihood ratio, CBD=common bile duct, NPV=negative predictive value, PPV=positive predictive value.

93.3%, specificity of 81.3% to 96%, PPV of 75.7%, and NPV of 91.5%.^[10,23] The IOC has a sensitivity of 76% to 100% and a specificity of 96% to 100% in the diagnosis of choledocholi-thiasis.^[8] Although both methods have similar sensitivity and specificity, the IOC has the advantage that it can only be performed during cholecystectomy, which can reduce waiting days for surgery and the hospital stay by eliminating the time interval between the study and the surgery. In our study, this advantage allowed us to reduce the average of hospital stay almost by 2 days.

The indication of early ERCP for patients with ABP and related cholangitis is well established, but its role and timing in case of mild ABP without signs of cholangitis remains controversial.^[6] It is important to understand that ABP and choledocholithiasis are dynamic pathologies, in which the continuous evaluation of the evolution, risk of choledocholithiasis, and severity of the pancreatitis is essential to perform the most accurate treatment in each patient.

As we mentioned before, it has been described that more than 50% of the CDB stones in acute pancreatitis pass spontaneously into the duodenum,^[6,9–11] but the time of migration varies widely.^[7,24] We decided to wait 48 hours before sending the patients with ABP and a high probability of choledocholithiasis to ERCP; 15 (46.8%) patients changed from high probability to intermediate probability of choledocholithiasis and only 2 (13.3%) of these patients were diagnosed with choledocholithiasis; therefore 13 (40.62%) of 32 patients who were classified with a high probability of choledocholithiasis at admission did not present common bile duct stones at the time of the image study. This does not necessarily mean that there was a spontaneous passage of stones in 40.62% of our patients, but that waiting 48 hours to make the decision to send a patient to ERCP for re-evaluation could prevent unnecessary procedures.

5. Conclusions

It is important to emphasize that the timing for cholecystectomy and the diagnostic method of choledocholithiasis depends in many cases on the resources of each hospital. We suggest an IOC as the election method for the diagnosis of CBD stones in patients with mild ABP in medical centers similar to ours because it reduces waiting days for surgery and hospital stay compared with the MRC.

This is a short-term, nonrandomized, prospective study with only 47 patients evaluated; randomized trials should be performed comparing MRC and IOC and its impact on the length of waiting days for surgery and the hospital stay, and also the advantages of re-evaluating the probability of choledocholithiasis 48 hours after inpatient admission.

Author contributions

Conceptualization: Gustavo Angel Gómez-Torres, Jaime González-Hernández, Odeth Sherlyne Ortega-García, Francisco Manuel Abarca-Rendon, Liliana Faviola De la Cerda-Trujillo. **Data curation:** Gustavo Angel Gómez-Torres, Jaime González-

- Hernández, Carlos Rene López-Lizárraga, Eliseo Navarro-Muñiz, Francisco Manuel Bonnet-Lemus, Francisco Manuel Abarca-Rendon, Liliana Faviola De la Cerda-Trujillo.
- Formal analysis: Gustavo Angel Gómez-Torres, Jaime González-Hernández, Carlos Rene López-Lizárraga, Eliseo Navarro-Muñiz, Odeth Sherlyne Ortega-García, Francisco Manuel Bonnet-Lemus, Francisco Manuel Abarca-Rendon, Liliana Faviola De la Cerda-Trujillo.
- Funding acquisition: Gustavo Angel Gómez-Torres.
- Investigation: Gustavo Angel Gómez-Torres.
- Methodology: Gustavo Angel Gómez-Torres, Liliana Faviola De la Cerda-Trujillo.
- Supervision: Gustavo Angel Gómez-Torres.
- Validation: Gustavo Angel Gómez-Torres.
- Writing original draft: Gustavo Angel Gómez-Torres, Odeth Sherlyne Ortega-García.
- Writing review & editing: Gustavo Angel Gómez-Torres, Odeth Sherlyne Ortega-García.
- Gustavo Angel Gómez-Torres orcid: 0000-0002-5945-7238.

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