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, MDa,⋆, Jaime González-Hernández, MDb, Carlos Rene López-Lizárraga, MDb, Eliseo Navarro-Muñiz, MDb, Odeth Sherlyne Ortega-García, MDb, Francisco Manuel Bonnet-Lemus, MDb, Francisco Manuel Abarca-Rendon, MDb, Liliana Faviola De la Cerda-Trujillo, PharmDh

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 (±2.69) days compared with 6.43 (±2.57) days in the group 2 (IOC) (P = .007). Mean waiting days for cholecystectomy was 17.14 (±26.04) days for group 1 and 5 (±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.[1] The gallstone disease is the most frequent etiology of acute pancreatitis representing 30% to 50%.[2–4] Acute biliary pancreatitis (ABP) results from the 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.[3,8]

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.[2,4,11–15] 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.
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, and the probability of choledocholithiasis was calculated according to the ASGE guidelines. 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 > 6 mm; 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 (±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 (±10.2) years; choledocholithiasis was diagnosed in 1 (4.3%) patient.

The waiting time for the MRC group was of 4.9 (±1.47) days and of 5 (±2.69) days for the IOC group, and there was no
Table 1
Characteristics of the type of patients.

| Type | Patients | Type 1 | Type 2 | Type 3 |
|------|----------|-------|-------|-------|
| Female sex, no. (%) | 11 | 9 (82%) | 11 (85%) | 23 (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 bilirubin at admission, mg/dL | 1.6 (±1.2) | 4.06 (±2.3) | 2.5 (±1.7) | |
| Decrease of total bilirubin, % mg/dL | 37.12 (±7.05) | 59.6 (±21.91) | 44.41 (±33.04) | |
| GGT admission, U/L | 198 (±54.6) | 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. % | 0 (0%) | 1 (7%) | 1 (4.3%) | |
| Cholecodocholithiasis, no. % | 33% | 36% | 46% | |
| Waiting days for MRC or IOC, d | 4.8 (±1.4) | 5 (±1.5) | 5 (±2.69) | |
| Waiting days for surgery, d | 27.4 (±25.6) | 7.8 (±3.8) | 5 (±2.69) | |
| Hospital stay, d | 7.6 (±1.28) | 8.8 (±3.4) | 6.4 (±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.

Table 2
Statistical differences between the groups.

|                | Group 1 CMR | Group 2 IOC | P     |
|----------------|-------------|-------------|-------|
| 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 bilirubin at admission, mg/dL | 2.96 (±2.21) | 2.5 (±1.78) | .67 |
| Decrease of total bilirubin, % mg/dL | 52.12 (±25.52) | 44.41 (±33.04) | .72 |
| GGT admission | 318.25 (±229.3) | 200.56 (±185.22) | .04 |
| ALP admission | 203.66 (±229.3) | 152.13 (±55.77) | .11 |
| High probability of choledocholithiasis | 10 (41%) | 5 (21%) | .4 |
| Admission, no. % |       |       |       |
| Cholecodocholithiasis, no. % | 2 (8%) | 1 (4%) | .16 |
| Waiting days for MRC or IOC, d | 4.9 (±1.47) | 5 (±2.69) | .25 |
| Waiting days for surgery, d | 17.14 (±26.04) | 5 (±2.69) | .001 |
| Hospital stay, d | 8.29 (±2.69) | 6.43 (±2.57) | .007 |

Means SD (±); statistically significant (P < 0.05).

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.13,16 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.17-21 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 23% to 76.1%.19-23 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 Narvaez-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...
93.3%, specificity of 81.3% to 96%, PPV of 75.7%, and NPV of 91.5%. The IOC has a sensitivity of 76% to 100% and a specificity of 96% to 100% in the diagnosis of choledocholithiasis. 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. 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, but the time of migration varies widely. 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.

Table 3

Diagnostic performance of ASGE high probability criteria and their individual predictors for choledocholithiasis.

| 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 >62 U/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.

Author contributions

Conceptualization: Gustavo Angel Gómez-Torres, Jaime González-Hernández, Odethe 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, Odethe 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.

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.

References

[1] León-Espinosa C, Bordo S, Lopez-Sebastian J, et al. What guidelines tell us about acute pancreatitis. A review of the last international guidelines. Open Med [Internet] 2014;9:

[2] Navarro-Sánchez A, Ashrafian H, Lalitot A, et al. Single-stage laparoscopic management of acute gallstone pancreatitis: outcomes at different timings. Hepatobiliary Pancreat Dis Int 2016;15:297–301.

[3] El-Dhuweib Y, Deakin M, David G, et al. Definitive management of gallstone pancreatitis in England. Ann R Coll Surg Engl 2012;94:402–6.

[4] Lee SL, Jarmin R, Lim KF, et al. Outcomes of early versus delayed cholecystectomy in patients with mild to moderate acute biliary pancreatitis: a randomized prospective study. Asian J Surg 2018;41:47–54.

[5] Park JG, Kim KB, Han J-H, et al. The usefulness of early endoscopic ultrasonography in acute biliary pancreatitis with undetectable choledocholithiasis on multidetector computed tomography. Korean J Gastroenterol 2016;68:202.

[6] Anderloni A. Role and timing of endoscopy in acute biliary pancreatitis. World J Gastroenterol 2015;21:11205.

[7] Cavarà F, Yildar M, Telligoli G, et al. Controversial issues in biliary pancreatitis: when should we perform MRCP and ERCP? Pancreatology 2014;14:411–4.

[8] Gurusamy KS, Giljaca V, Takwoingi Y, et al. Endoscopic retrograde cholangiopancreatography versus intraoperative cholangiography for diagnosis of common bile duct stones. Cochrane Database Syst Rev 2015;2:CD010339.
[9] Lefemine V, Morgan RJ. Spontaneous passage of common bile duct stones in jaundiced patients. Hepatobiliary Pancreat Dis Int 2011;10:209-13.

[10] Lee S-L, Kim H-K, Choi H-H, et al. Diagnostic value of magnetic resonance cholangiopancreatography to detect bile duct stones in acute biliary pancreatitis. Pancreatology 2018;18:22-8.

[11] Tranter S, Thompson M. Spontaneous passage of bile duct stones: frequency of occurrence and relation to clinical presentation. Ann R Coll Surg Engl 2003;85:174-7.

[12] Maple JT, Ben-Menachem T, Anderson MA, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. Gastrointest Endosc 2010;71:1-9.

[13] Egin S. Early laparoscopic cholecystectomy following acute biliary pancreatitis expedites recovery. Turk J Trauma Emerg Surg 2017;23:495-500.

[14] Aksoy F, Demiral G, Ekinci O. Can the timing of laparoscopic cholecystectomy after biliary pancreatitis change the conversion rate to open surgery? Asian J Surg 2017;41:307-12.

[15] de Mestral C, Hoch JS, Laupacis A, et al. Early cholecystectomy for acute cholecystitis offers the best outcomes at the least cost: a model-based cost-utility analysis. J Am Coll Surg 2016;222:185-94.

[16] Hwang SS, Li BH, Haigh PL. Gallstone pancreatitis without cholecystectomy. JAMA Surg 2013;148:867.

[17] Uhl W, Warshaw A, Imrie C, et al. IAP guidelines for the surgical management of acute pancreatitis. Pancreatology 2002;2:565-73.

[18] Tenner S, Bailie J, DeWitt J, et al. American College of Gastroenterology Guideline: management of acute pancreatitis. Am J Gastroenterol 2013;108:1400-15.

[19] Nárvaez Rivera RM, González González JA, Montreal Robles R, et al. Accuracy of ASGE criteria for the prediction of choledocholithiasis. Rev Esp Enfermedades Dig 2016;108:309-14.

[20] Kang J, Paik K, Lee J, et al. The efficacy of clinical predictors for patients with intermediate risk of choledocholithiasis. Digestion 2016;94:100-5.

[21] Kuzu UB, Odemir B, Dışebeyaz S, et al. Management of suspected common bile duct stone: diagnostic yield of current guidelines. HPB (Oxford) 2017;19:126-32.

[22] He H, Tan C, Wu J, et al. Accuracy of ASGE high-risk criteria in evaluation of patients with suspected common bile duct stones. Gastrointest Endosc 2017;86:525-32.

[23] Giljaca V, Gurusamy KS, Takwoingi Y, et al. Endoscopic ultrasound versus magnetic resonance cholangiopancreatography for common bile duct stones. Cochrane Hepato Biliary Group. Cochrane Database Syst Rev 2015;26:CD0011549.

[24] Frossard JL, Hadengue A, Amouyal G, et al. Choledocholithiasis: a prospective study of spontaneous common bile duct stone migration. Gastrointest Endosc 2000;51:173-9.