

Endoscopic Retrograde Cholangiopancreatography (ERCP) in Acute Biliary Pancreatitis (ABP) either with or without Concomitant Cholangitis

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ABSTRACT

BACKGROUND AND AIM: The use of endoscopic retrograde

cholangiopancreatography (ERCP) in acute biliary pancreatitis (ABP) without cholangitis is very debatable. This work aimed to compare the impact of ERCP on the outcome of ABP with or without cholangitis.

METHOD: Patients underwent ERCP for ABP were included and classified to two groups, group A with concomitant cholangitis and B without cholangitis. Data from both groups were analyzed and compared at baseline and post-ERCP ($p < 0.05$).

RESULT: Group A ($n = 46$) showed insignificantly higher median age and less female distribution than B ($n = 32$) (37 vs. 36 years) and (69% vs. 43%) respectively. Serum bilirubin and AST were significantly higher in group A than B (5.9 vs. 1.9 mg/dl) & (172 vs. 136 U/L) respectively. The other baseline variables: ALT, ALP, amylase, lipase, CRP and pain score had insignificant difference. Cannulation time was significantly shorter in group A vs. B (9 vs. 16 minutes, $p = 0.01$). Post-ERCP there was statistically significant difference in the medians of serum bilirubin (2 vs. 1.4 mg/dl), amylase (121 vs. 496) and CRP (57 vs. 33 mg/dl) while the rest of variables had statistically insignificant difference. Pain score did not improve in 8 patients (17%) in group A vs. 12 (37%) in B ($p = 0.04$) but the overall outcome showed no significant difference. AST, ALP, bilirubin, amylase and pain score have significantly improved in group B pre and post-ERCP.

CONCLUSION: ERCP is safe procedure in ABP with or without cholangitis, with no statistically significant difference regarding the clinical and biochemical outcomes.

Key words: ERCP; Biliary Pancreatitis; Cholangitis

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Abbreviations

ERCP	Endoscopic Retrograde Cholangiopancreatography
ABP	Acute Biliary Pancreatitis
AP	Acute Pancreatitis
US	Abdominal Ultrasound
CT	Computerized Tomography
CBDS	Common Bile Duct Stone(s)
WGC	Wire-Guided Cannulation
TPP	Trans-Papillary Papillotomy
TPF	Trans-Papillary Fistulotomy
DGT	Double Guide-wire Technique
EUS	Endoscopic Ultrasound

INTRODUCTION

Acute pancreatitis (AP) is the most common pancreatic disease worldwide with increasing incidence but decreasing death rate to less than 2% in recent years^[1,2]. Biliary stones, alcohol consumption, iatrogenic causes, metabolic disorders, autoimmunity, infections and pancreatic neoplasms are the commonly known aetiologic factors^[3], however; wide number of cases are recorded as idiopathic AP.

The diagnosis of AP requires at least 2 of the following features: characteristic abdominal pain; biochemical evidence of pancreatitis; and/or radiographic evidence of pancreatitis on cross-sectional imaging^[4]. The disease has a wide array of clinical presentations which may be mild with full recovery after receiving the proper treatment or severe causing various local and systemic complications that may end in death if not properly managed^[5,6].

Acute biliary pancreatitis (ABP) is the most common form of AP, develops as a result of transient obstruction of the bile duct and pancreatic duct with subsequent bile reflux into the pancreatic duct or increase in its hydrostatic pressure^[7]. Biliary aetiology of AP can be suggested when alanine transaminase (ALT) level shows a threefold elevation with a 95% positive predictive value^[8,9].

The use of endoscopic retrograde cholangiopancreatography (ERCP) as a therapeutic tool in patients with ABP is very controversial regarding its role, time and safety^[10-13]. The aim of this work was to study the impact of performing ERCP within 24-hour of the onset of ABP on its clinical outcome.

METHOD**1. Patients**

Patients presented with confirmed ABP from March 1, 2018 till June 30, 2019 were prospectively included and subjected to ERCP procedure after full clinical and investigational work up as per the policy of our center. Diagnosis of ABP was based on presence of deep-seated epigastric pain, at least triple-fold rise of pancreatic amylase and/or lipase, and radiologic findings of AP including edema, fluid collection or necrosis as detected by abdominal ultrasound (US) and computerized tomography (CT). Biliary aetiology of AP was confirmed by a triple-fold rise of ALT with detection of common bile duct stone(s) (CBDS) or mud in abdominal imaging. Patients with AP of non-biliary aetiology as well as patients with unidentified cause of AP after both US and CT were initially excluded. Also; patients with history of previous pancreatitis, chronic pancreatitis and alcoholics were excluded.

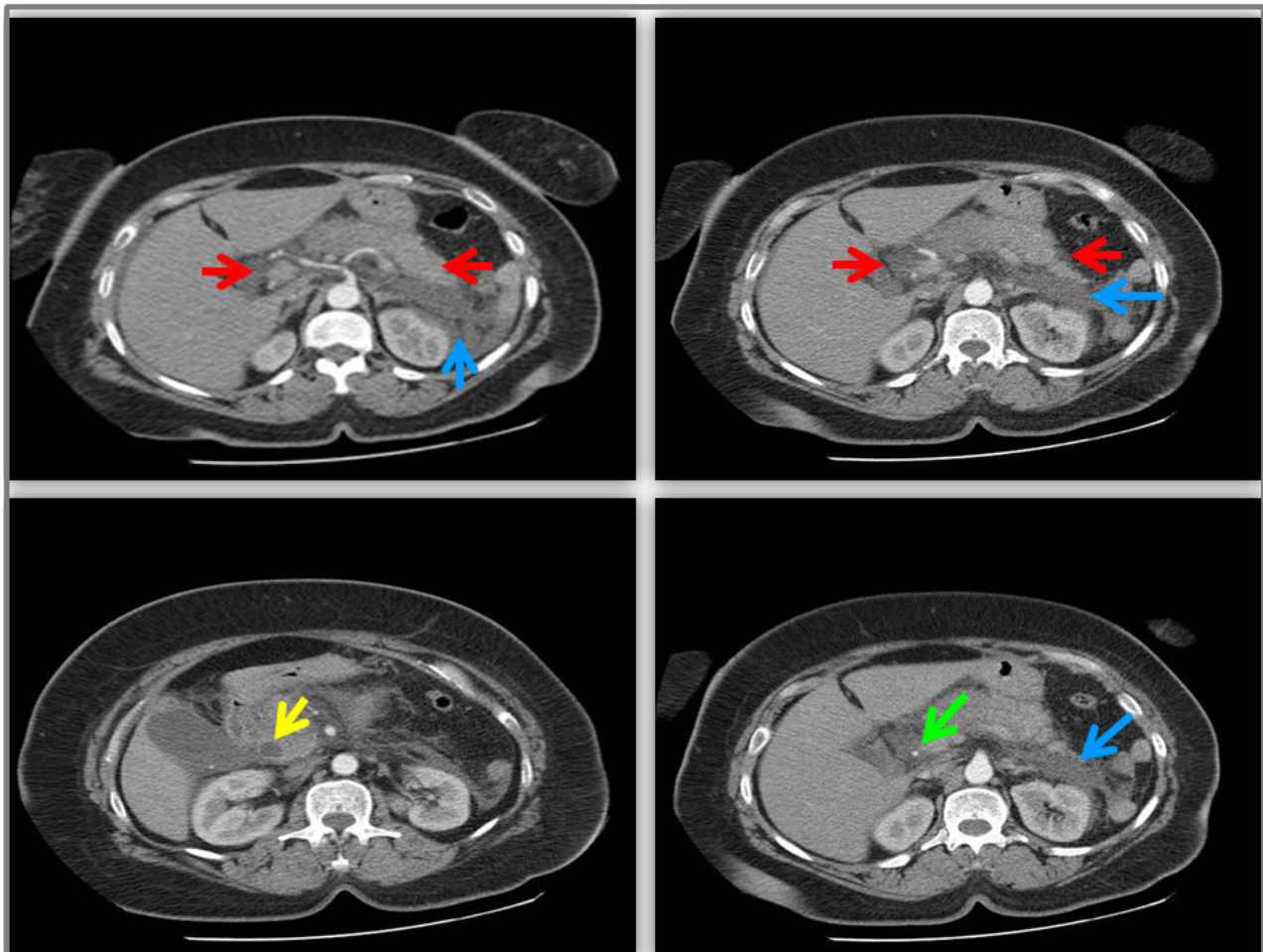


Figure 1 Typical CT findings in ABP patient with diffusely enlarged pancreas and hazy surrounding fat plans (red arrows), free intra-abdominal collection (blue arrows), dilated pancreatic part of the CBD (yellow arrow) till the level of an obstructing calcified small stone impacted at its distal part (green arrow).

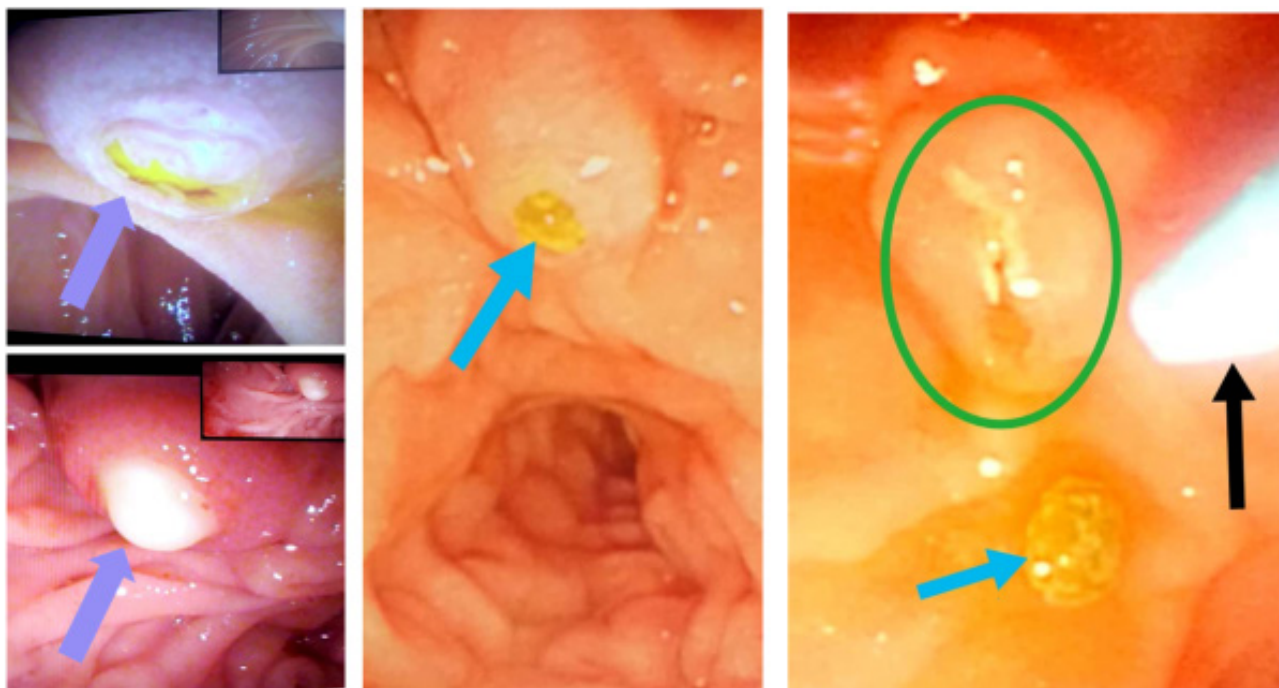


Figure 2 Impacted stones at the papillary orifice (blue arrows) and the appearance of the papilla (green circle) after achieving biliary access via transpapillary papillotomy and stone extraction.

Table 1 Comparison between the studied groups before ERCP. Statistically significant difference between studied groups in AST, total and direct bilirubin.

Variables	Group A (n = 46) With Cholangitis	Group B (n = 2) Without Cholangitis	p-value	
Age	37 (31.7-47.5)	36 (33-43.7)	0.4	
Females (%)	20 (43%)	22 (69%)	0.02	
ALT (U/L)	226.5 (106.5-392)	198 (100-276)	0.1	
AST (U/L)	172 (98-270)	136.5 (76-178)	0.03	
ALP (U/L)	228 (99.7-456)	220.5 (190-233)	0.8	
T. Bilirubin (mg/dl)	5.9 (4.3-7.3)	1.9 (1.3-2.1)	0.01	
D. Bilirubin (mg/dl)	3.9 (3.1-5.1)	0.7 (0.5-0.9)	0.01	
Amylase (U/L)	573 (264.5-1272)	905 (328-1551)	0.5	
Lipase (U/L)	471 (260-2453)	537 (359-862)	0.6	
TLC (x10 ³ /ul)	11.7 (9-14.8)	14.5 (10.5-17.5)	0.2	
Hb (g/dl)	14 (13-15)	13 (11.5-14)	0.06	
Platelets (x10 ³ /ul)	292 (220-332)	327 (209-359)	0.1	
CRP (mg/dl)	79 (32-102)	54 (35-68.7)	0.07	
Pain Score	Mild	8 (17.4%)	10 (31.3%)	0.1¶
	Moderate	30 (65%)	20 (62.5%)	
	Sever	8 (17.4%)	2 (6.3%)	
BISAP Score	≤ 2	44 (96%)	29 (91%)	
	> 2	2 (4%)	3 (9%)	

Mann-Whitney test unless indicated, ¶: Chi squared test.

To distinguish patients with concomitant cholangitis from those without cholangitis, the included patients were then classified into two groups: group (A) with concomitant cholangitis as defined as right upper quadrant pain, serum bilirubin ≥ 3 mg/dl and temperature ≥ 38°C, and group (B) patients without cholangitis who did not fulfill these criteria.

2. ERCP Procedure

ERCP procedures were performed within 24-hour of the onset of pain by experienced ERCP endoscopists with more than 500 procedures

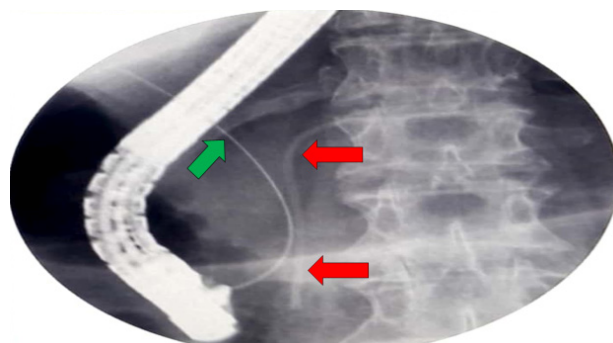


Figure 3 The guidewire passing through the CBD (green arrow) after insertion of pancreatic duct plastic stent (red arrow).

Table 2 comparison between studied groups as regard ERCP procedure. Statistically significant difference between studied groups as regard Cannulation time.

		Group A (n = 46) With Cholangitis	Group B (n = 32) Without Cholangitis	p-value
Cannulation	WGT	30 (65.2%)	24 (75%)	0.3¶
	TPF	12 (26%)	6 (19%)	
	TTP	1 (2.2%)	2 (6%)	
	DGT	3 (6.5%)	0 (0%)	
Cannulation time (min)		9.3 (7-11)	16.5 (8-18)	0.01
Total Procedure time (min)		65 (55-74)	73.8 (57.5-86.7)	0.1
CBD diameter (mm)		11 (8.7-12.5)	10 (9-12)	0.3

Mann-Whitney test unless indicated, ¶: Chi squared test.

performed, the used scope was Olympus TJF 260V. All procedures were performed under propofol anesthesia and cardiopulmonary monitoring. Details of the ERCP procedure including cannulation time, cannulation technique, distal CBD diameter, detection/ extraction of CBDS or microlithiasis, placement of biliary or pancreatic stent, and total procedure time were recorded. A written

informed consent was obtained from all included patients before the procedure. All patients were received pre-procedure intramuscular diclophenate and subjected to close clinical and laboratory follow up till the time of discharge.

3. Statistical Analysis

Categorical variables are expressed as number and percent, continuous variables as medians and interquartile ranges 25 and 75 (IQRs). Chi squared test was used to compare non-parametric variables and Mann Whitney test was used to compare continuous variables. Analysis was performed using SPSS[®], version 22, $p < 0.05$ was considered statistically significant.

4. Ethical Clearance

The study protocol was concomitant with the ethical guidelines of the 1975 Declaration of Helsinki and approved by the ethical committee of Qena Faculty of Medicine, South Valley university, Qena, Egypt.

RESULT

A total of 78 ABP patients were included, with median age: 37 years (IQRs: 33-46), females were 42 (54%). At presentation; all patients had deep seated epigastric pain typical of acute pancreatitis (AP). BIASP score was calculated and recorded to all patients at the time of admission.

Patients who fulfilled criteria of acute cholangitis were included in group A ($n = 46$), while those who were not fulfill it were included in group B ($n = 32$). Table 1 shows comparison between both groups at baseline. Group A showed higher median age (37 years) and less female distribution (43%) than group B (36 years) and (69% females) with no statistically significant difference ($p = 0.4$) and (0.02) respectively. Serum bilirubin and AST were statistically higher in group A (5.9 mg/dl) and (172 U/L) than in group B (1.9 mg/dl) and (136 U/L) respectively. The other baseline variables including ALT, ALP, amylase, lipase and CRP had no statistically significant difference between the two groups with medians of 226 vs. 198 U/L, 228 vs. 220 U/L, 573 vs. 905 U/L, 471 vs. 537 U/L, 79 vs. 54 mg/dl respectively. The severity of pain showed no statistically significant difference ($p = 0.1$) in both groups with 17% vs. 31% had mild pain, 65% vs. 62% had moderate-intensity pain and 17% vs. 6% had severe pain in group A&B respectively.

Figure 1 shows an example from the included patients with typical CT findings of ABP in the form of diffuse pancreatic enlargement, haziness of the peripancreatic fat plans, free intra-abdominal collection extending to the lesser sac, and dilated CBD with an obstructing calcified small stone at its distal part.

Details of ERCP procedures in both groups are shown in table 2 which shows statistically significant shorter cannulation time in group A vs. B (median: 9 vs. 16 minutes; $p = 0.01$), however the cannulation technique, CBD diameter and total procedure time did not show any statistically significant difference. An impacted stone at the papillary orifice was the leading cause of AP in 3 cases of our series (1 in group A and 2 in group B), all were managed by transpapillary papillotomy (Figure 2). Pancreatic stenting was required in one case in group A because of frequent passage of the wire and contrast injection into the pancreatic duct (Figure 3).

Table 3 shows comparison between the two groups post-ERCP with statistically significant difference in the medians of serum bilirubin (2 vs. 1.4 mg/dl, $p = 0.01$), amylase (121 vs. 496, $p = 0.01$) and CRP (57 vs. 33 mg/dl, $p = 0.04$). The rest of variables including ALT, AST, ALP and lipase had statistically insignificant difference.

Table 3 Comparison between the studied groups after ERCP. Statistically significant difference between studied groups as regard total, direct bilirubin, CRP and amylase

Variables	Group A ($n = 46$)	Group B ($n = 32$)	P-value
	With Cholangitis	Without Cholangitis	
ALT (U/L)	114.5 (77-258.7)	147.5 (76.5-207.5)	0.8
AST (U/L)	82.5 (59-105)	93 (46-138)	0.9
ALP (U/L)	180 (88.5-227)	133 (105.5-187.5)	0.4
T. Bilirubin (mg/dl)	2.1 (1.2-3.6)	1.4 (1.1-1.6)	0.01
D. Bilirubin (mg/dl)	1.2 (0.8-2.1)	0.8 (0.6-1)	0.01
Amylase (U/L)	121 (75.5-250)	496 (289.5-698.5)	0.01
Lipase (U/L)	287 (125.5-429)	390 (274.7-705.7)	0.1
TLC ($\times 10^3$ /ul)	11 (8-12.9)	12.6 (7.7-15)	0.1
Hb (g/dl)	14 (12-15)	11.7 (11-14)	0.08
PLT ($\times 10^3$ /ul)	299 (225-341)	281.5 (194-313)	0.2
CRP (mg/dl)	57 (23-83)	33 (16.7-64.5)	0.04
Pain	8 (17%)	12 (37%)	0.04 [¶]
Overall Outcome	Improved	46 (100%)	30 (94%)
	Not-improved	0 (%)	2 (6%)

Mann-Whitney test unless indicated, [¶]: Chi squared test.

Table 4 Comparison before and after ERCP in group B. Statistically significant difference between AST, ALP, T. Bilirubin and amylase (before and after ERCP).

Variables	Group B before ERCP ($n = 32$)	Group B after ERCP ($n = 32$)	p-value
ALT (U/L)	198 (100-276)	147.5 (76.5-207.5)	0.1
AST (U/L)	136.5 (76.5-178)	93 (46-138)	0.03
ALP (U/L)	220.5 (190-233)	133 (105.5-187.5)	0.01
T. Bilirubin (mg/dl)	1.9 (1.3-2.1)	1.35 (1- 1.6)	0.01
D. Bilirubin (mg/dl)	0.7 (0.5-0.9)	0.8 (0.6-1)	0.9
Amylase (U/L)	905 (328-1551)	496 (289.5-698.5)	0.006
Lipase (U/L)	537 (359.5-862)	390 (274.7-705.7)	0.1
TLC ($\times 10^3$ /ul)	14.5 (10.5-17.5)	12.6 (7.7-15)	0.3
Hb (g/dl)	13 (11.5-13.7)	11.7 (10.7-14)	0.2
PLT ($\times 10^3$ /ul)	327 (209-359)	281.5 (194-313)	0.05
CRP (mg/dl)	54 (35-69)	33 (17-64.5)	0.08
Pain Score	No	0 (0%)	0.01 [¶]
	Mild	10 (31.3%)	
	Moderate	20 (62.5%)	
	Sever	2 (6.3%)	

Mann-Whitney test unless indicated, [¶]: Chi squared test.

Pain score showed improvement in all group A patients except in 8 patients (17%) while 12 patients (37%) in group B did not achieve improvement of their pain ($p = 0.04$) 24-hour post-ERCP. The overall outcome has improved in all group A patients while only 2 patients (6%) in group B showed persistent pain and worse general condition for 72-hour post-ERCP but then improved after proper medical treatment.

Comparison of group B before and after ERCP is shown in table 4 which shows statistically significant improvement in the level of AST, ALP, bilirubin and amylase with p-values of 0.03, 0.01, 0.01 and 0.006 respectively. Pain score has significantly improved post-ERCP ($p = 0.01$), before ERCP; 10 patients had mild pain, 20 had moderate and 2 had severe pain while post-ERCP 20 patients (62.5%) were pain free and 12 (37.5%) had mild pain; 10 of them were improved within 24-hour while 2 have required 72-hour hospitalization and additional medical treatment.

DISCUSSION

Acute biliary pancreatitis is caused by transient obstruction of the bile and pancreatic duct with subsequent reflux of the biliary and duodenal contents in the pancreatic duct and/or increases in its hydrostatic pressure that yields pancreatic necrosis with increasing severity when the duration of obstruction exceeds 48 hours^[14]. Initial surgical decompression of the bile duct after the diagnosis of pancreatitis has been tried in previous studies^[15,16] but the outcome was not satisfactory due to high mortality rate in the urgent surgery group. On the other hand; endoscopic management using ERCP was tried in three later studies with favorable outcome in Neoptolemos *et al*^[17] and Fan *et al*^[18], and unbeneficial effect in Fölsch *et al*^[19].

Putting in mind ERCP is a very challenging endoscopic procedure with a substantial risk of procedure related complications and it becomes technically more difficult in the sitting of AP due to presence of oedema of the duodenal wall and papilla^[20], the AGA Guideline on Initial Management of AP 2018^[1,3] does not recommend the use of ERCP in ABP and confines its role only in presence of concomitant cholangitis or persistent biliary obstruction. On the other hand; the UK guideline for the management of acute pancreatitis indicates urgent therapeutic ERCP in all patients with severe pancreatitis and suspected biliary etiology or if there is cholangitis, jaundice or a dilated common bile duct^[21].

In a study conducted by Lee *et al*^[7] on 73 patients with ABP without concomitant cholangitis, ERCP procedure was performed either within less than 24 hours of presentation (urgent ERCP) in 39 patients or from 24-72 hours of presentation (early ERCP) in 34 patients, with no statistically significant difference in-between the two groups regarding technical success, clinical success and complication rate. Despite this study highlighted the safety of ERCP in the setting of ABP, the basis of performing ERCP either urgently or early was not clear. In the current study and to overcome this issue, all ERCP procedures were performed urgently (within the first 24 hours from the onset of pain), and patients with concomitant cholangitis were included in a separate group to compare them with those without cholangitis.

The value of ERCP in patients with ABP and associated cholangitis is well established^[22,23], however; its role in patients without cholangitis remains controversial. In the current study, abdominal pain and the related biochemical profiles have improved after ERCP either in patients with or without cholangitis with no statistically significant difference in the overall outcome. Despite the possible normal evolution of both clinical and biochemical profiles, we think ERCP may has a valuable desired contribution in achieving biliary decompression and minimizing inflammation.

As ERCP is not recommended as a pure diagnostic procedure due to the availability of other diagnostic maneuvers and a complication rate of 5-10%^[24], endoscopic ultrasound (EUS) screening for choledocholithiasis is the more advantageous strategy in severe ABP with lower costs and fewer ERCP-related and procedure related complications^[25,26]. In a recent systematic review^[27] included seven studies with a total of 545 ABP patients, De Lisi *et al* concluded that early EUS in patients with ABP can exclude the presence of CBDS without adding risks and avoid further invasive examinations in compromised patients. On the contrary, if a stone is detected, ERCP can be performed in the same session; altogether an EUS-based management of patients with ABP results in a safer and more effective strategy^[27]. However; echoendoscopes and skilled endosonographers are not available except in tertiary centers.

Our work is one-arm single-center study neither include

comparison with non-intervention group nor comparison with another center or another endoscopist experience. Also; it lacks cost-benefit analysis. In conclusion; ERCP is safe and useful procedure for ABP patients either with or without concomitant cholangitis with no statistically significant difference in the overall outcome in-between.

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