Optimal Timing of Endoscopic Intervention After Extracorporeal Shock-Wave Lithotripsy in the Treatment of Chronic Calcified Pancreatitis

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Objectives: The interval between extracorporeal shock-wave lithotripsy (ESWL) and endoscopic retrograde cholangiopancreatography (ERCP) may cause differences in cannulation and stone removal. This study was to investigate the optimal timing of ERCP after ESWL.

Methods: Patients with chronic calcified pancreatitis, who underwent ESWL and subsequent ERCP in Changhai Hospital from February 2012 to February 2015, were retrospectively analyzed. The interval between ESWL and ERCP was used to divide patients into groups A (<12 hours), B (12–36 hours), and C (>36 hours). Cannulation success, stone clearance, and post-ESWL/ERCP complications were compared.

Results: A total of 507 patients were enrolled. There were no significant differences regarding the successful cannulation and stone removal rates between the 3 groups. In patients without prior ERCP, the successful cannulation rates were 71.4%, 81.9%, and 90.9% ($P = 0.004$), and the successful clearance rates were 76.2%, 85.1%, and 90.9% ($P = 0.031$) for these 3 groups, respectively, showing significant differences. There were no differences in the successful cannulation and stone extraction rates for patients with prior ERCP.

Conclusions: The interval between ESWL and ERCP in chronic calcified pancreatitis patients with prior ERCP is not relevant, while delaying endoscopic intervention is recommended in those with native papilla.

Key Words: cannulation, chronic calcified pancreatitis, ERCP, stone clearance

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Chronic pancreatitis (CP) is a disease of the pancreas in which recurrent inflammation results in fibrous connective tissue replacing the pancreatic parenchyma. Progressive damage of the pancreatic parenchyma causes failure of exocrine and endocrine pancreatic function.[1] The incidence of CP worldwide is reported to be between 1.6 and 23 per 100,000, with an increasing global prevalence.[1,2] Chronic pancreatitis is characterized by the formation of pancreatic stones, which reportedly develop in 32% to 90% of patients.[3,4] Calcifications can develop in up to 90% of patients with alcoholic CP (ACP), one of the most common etiologies of chronic calcified pancreatitis (CCP),[5] during long-term follow-up.[6]

Pain is the main symptom of CCP. The severity and complications of the pain associated with CCP significantly reduces the quality of life and life expectancy of patients.[7,8] The mechanism of pain in CCP is poorly understood and is likely multifactorial. The obstruction of pancreatic juice by stones in the main pancreatic duct (MPD) causes hypertension of the pancreatic duct and pancreatic parenchyma, resulting in hypoperfusion and ischemic injury of the acinar cells,[9–11] which are believed to be the main causes of pain. Thus, decompression of the MPD by removing stones can greatly relieve pain and improve clinical symptoms.[4,5] Both surgical and endoscopic interventions to manage the pain from obstructive CCP have been proven effective, while the latest guidelines recommend endoscopy and extracorporeal shock-wave lithotripsy (ESWL) as first-line therapies for painful uncomplicated CCP.[12,13] Patients with CCP and pancreatic stones of 5 mm or greater obstructing the pancreatic duct can undergo ESWL for stone fragmentation. It is routinely followed by stone extraction via endoscopic retrograde cholangiopancreatography (ERCP),[4,12] which has been proven safe and effective, even in pediatric patients.[14,15] However, ESWL and ERCP can yield adverse events. Major complications associated with ESWL are post-ESWL pancreatitis, bleeding, infection, steinstrasse, and perforation.[16] Other studies have reported rare complications such as gastric submucosal hematoma[17] and mesenteric hematoma after ESWL.[18] These complications may affect the success of selective deep cannulation and stone clearance under subsequent endoscopic treatment.

Complete duct clearance was associated with a better pain reduction.[19] Endoscopic clearance of stones in CCP patients has been more successful in clearing solitary stones, stones located in the pancreatic head, and stones at a density of less than 820.5 Hounsfield units on a computed tomography scan and when a pancreatic stent has been inserted before ESWL.[20–22] Cannulation of the MPD under ERCP can be a technical challenge even to endoscopists experienced in pancreatobiliary endoscopy. Successful cannulation of major papilla has been reported in 90% to 98% of cases, whereas failure rates of minor papilla cannulation are in the range of 5% to 10%.[23] Risk factors for cannulation failure during ERCP in CCP patients include pancreatic duct strictures, stones, a pancreatic duct with a loop configuration, surgically altered anatomy, and pancreas divisum.[23–25] Early complications after ERCP in patients with CCP include post-ERCP pancreatitis (PEP), bleeding, infection, and perforation.[26,27] Post-ERCP pancreatitis is the most common and severe complication after ERCP. Various mechanisms have been proposed as the cause of PEP in terms of pancreatic

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injury and early activation of pancreatic enzymes, including mechanical trauma, chemical injury, hydrostatic injury, and infection.[28,29] The risk factors for PEP include female sex, a history of acute pancreatitis or PEP, precut sphincterotomy, and difficult cannulation.[30–32]

Edema, which has been reported to be a result of the shock waves used in ESWL, may make cannulation and stone clearance of the MPD difficult during ERCP.[33] Papillary edema and pancreatic edema caused by ESWL increase the difficulty of cannulation in early ERCP, thereby increasing the risk of PEP.[34] Prolonging the timing of ERCP may relieve edema, thus improving the success of ERCP and reducing occurrence of PEP. A retrospective study reported that delayed ERCP was important to successfully clear stones from the MPD.[33] However, the optimal timing of ERCP after ESWL is still controversial. Given the potential relationship between the timing of ERCP after ESWL and the success of cannulation and stone clearance, as well as the subsequent occurrence of PEP, we wanted to investigate the optimal timing of ERCP after stone disintegration by ESWL.

MATERIALS AND METHODS

Study Design and Patients

All patients between 18 and 75 years of age who underwent ESWL followed by ERCP for CCP between February 2012 and February 2015 at the Digestive Endoscopy Center of Changhai Hospital were retrospectively included, regardless of previous endoscopic treatment. Patients with a history of pancreatic surgery or gastrectomy with Billroth II reconstruction, suspected malignant tumors, or contraindications to ESWL or ERCP (eg, abdominal aortic aneurysm, pregnancy) were excluded. All patients treated with ESWL after admission to the hospital were evaluated with conventional ultrasound, endoscopic ultrasound, computed tomography, magnetic resonance imaging, or magnetic retrograde cholangiopancreatography to confirm the diagnosis of CCP and determine the duct diameter and the stone size and location before ESWL.[35,36] Extracorporeal shock-wave lithotripsy was performed for the clearance of radiopaque obstructive MPD stones larger than 5 mm located in the head/body of the pancreas as indicated in the guidelines.[11,12] The goal of ESWL was the complete or partial fragmentation of pancreatic duct stones as seen with fluoroscopy, allowing spontaneous or endoscopic duct clearance. The study involving human participants was approved by Changhai Institutional Review Board and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients gave the informed consent for analysis of the medical records during hospitalization.

Treatment Strategy

Extracorporeal shock-wave lithotripsy was performed by 2 endoscopists (H.C. and L.-H.H) using an electromagnetic lithotripter with the ability for bidimensional fluoroscopic targeting. Intravenous remifentanil combined with dexmedetomidine was administered for analgesia during the procedure. The fragmentation of the stones was monitored by fluoroscopy during the ESWL session. The vital signs of the patients were closely monitored, and procedure-related parameters, including intensity, frequency, duration, and fragmentation efficacy, were recorded by the endoscopists while performing ESWL. Extracorporeal shock-wave lithotripsy was repeated on consecutive days until the stones had been successfully fragmented, defined as stones broken into fragments of 2 mm or less to 3 mm, or X-rays demonstrated a decrease in stone density, an increase in stone surface area, and heterogeneity of the stones, which could fill the MPD and adjacent side branches.[12,21] Endoscopic retrograde cholangiopancreatography was performed after ESWL for painful CCP with an obstructed MPD in the head/body of the pancreas[11,12] to clear and visualize the MPD. The timing of ERCP was decided by the performing endoscopists, and it was usually less than 2 days after ESWL. Details about the anesthesia and the operation are provided in the Supplemental Digital Content (http://links.lww.com/MPA/A866).

To investigate the optimal interval between ESWL and ERCP, patients were divided into 3 groups depending on the interval they experienced: group A, less than 12 hours; group B, 12 to 36 hours; and group C, more than 36 hours, which meant that patients underwent endoscopic intervention on the same day as ESWL, the second day after ESWL, or more than 2 days after ESWL.

Outcomes

The primary outcomes were successful cannulation and successful clearance of MPD stones. Successful cannulation was defined as the completion of selective cannulation of the deep pancreatic duct.[34] Main pancreatic duct clearance was classified into complete clearance, defined as the fragmentation of the pancreatic stones to less than 3 mm and clearance of more than 90% of the fragments; partial clearance, defined as clearance of 50% to 90% of the fragments; and unsuccessful clearance, defined as the presence of pancreatic stones of more than 3 mm or clearance of less than 50% of the fragments. Successful clearance was defined as the complete or partial clearance of MPD stones.[37,38] For subgroup analysis, patients were further classified according to whether they had prior endoscopic treatment for CCP.

The secondary outcomes included post-ERCP and post-ESWL complications, as previously defined by Cotton et al.[39] Major post-ERCP complications included PEP, bleeding, infection, and perforation and were classified as mild, moderate, or severe, depending mainly on the length of hospitalization and the need for invasive treatment. Post-ESWL complications included acute pancreatitis, bleeding, infection, steinstrasse, and perforation and were also classified as mild, moderate, or severe.

Demographic information such as age; sex; the etiology of the CCP, including idiopathic CP, ACP, and hereditary CP; smoking; pancreatic duct morphology; location of stones; complications; and previous treatment obtained from electronic medical records was also collected and compared with the definitions presented in the Supplemental Digital Content (http://links.lww.com/MPA/A866). Pancreatic duct morphology was sorted into as 3 types: simple stones, stones with MPD stricture, and complex lesions (patients with stricture, stones, and also ductal dilatation in the body/tail area of pancreas).[40]

Statistical Analysis

The baseline characteristics of the 3 groups were compared using χ^2 and Wilcoxon tests. To analyze the primary and secondary endpoints, we used χ^2 tests or Fisher exact test to determine the differences in the successful cannulation rate and the successful rate of MPD stone clearance, with a final 2-tailed $P < 0.05$ indicating there was a statistical difference. Dichotomous data are presented as frequencies, and continuous data are presented as mean (standard deviation [SD]) or median and interquartile range. Multiple 2-group comparisons of the primary and secondary endpoints were assessed using a multiple-comparisons Bonferroni test. A P value (2-tailed) of <0.0167 was considered statistically significant.[41] Risk factors for successful cannulation and successful stone clearance were examined by univariate analysis, and those with $P < 0.15$ were included in a multivariable logistic regression analysis using the "Enter" method. Risk factors included in the final model are presented as odds ratios with 95% confidence intervals. All statistical analyses were performed using IBM SPSS Statistics version 23.0 (IBM Corp, Armonk, NY).

RESULTS

Baseline Characteristics

From February 2012 to February 2015, the records of 507 consecutive patients with CCP (368 [72.6%] were men and 139 [27.4%] were women) were retrospectively analyzed. The mean age of the patients was 43 (SD, 13.7) years. The main etiologies were as follows: 312 cases (61.5%) of idiopathic CP, 153 cases (30.2%) of ACP, and 22 cases (4.3%) of anatomic variants of the pancreatic duct.

Overall, 128 (25.2%), 161 (31.8%), and 218 (43.0%) patients underwent ERCP less than 12 hours after ESWL (group A), 12 to 36 hours after ESWL (group B), and more than 36 hours after ESWL (group C), respectively. Before admission to the hospital, 267 patients had not undergone a prior ERCP, and 240 patients had undergone a prior ERCP (eg, pancreatic sphincterotomy, dilatation of stricture, or stent placement) for painful CCP with an obstructed MPD in the head/body of the pancreas[11,12] and were readmitted because of a recurrence of symptoms or failure of the previous ERCP mainly due to large pancreatic stone of more than 5 mm.

The 3 groups were balanced with respect to their baseline characteristics (all $P > 0.05$) (Table 1).

TABLE 1. Baseline Characteristics of the Patients Analyzed

Characteristics, n (%)	Group A (n = 128)	Group B (n = 161)	Group C (n = 218)	*P*
Age, y				0.627
≤20	0 (0.0)	2 (1.2)	5 (2.3)	
21–40	29 (22.7)	44 (27.3)	58 (26.6)	
41–60	77 (60.2)	85 (52.8)	116 (53.2)	
>60	22 (17.2)	30 (18.6)	39 (17.9)	
Sex				0.096
Male	100 (78.1)	120 (74.5)	148 (67.9)	
Female	28 (21.9)	41 (25.5)	70 (32.1)	
Etiology				0.438
ICP	71 (55.5)	102 (63.4)	139 (63.8)	
ACP	46 (35.9)	50 (31.1)	57 (26.1)	
HCP	2 (1.6)	3 (1.9)	6 (2.8)	
Pancreas divisum	5 (3.9)	5 (3.1)	12 (5.5)	
Other*	4 (3.1)	1 (0.6)	4 (1.8)	
Smoking	67 (52.3)	90 (55.9)	118 (54.1)	0.833
Pancreatic duct morphology				0.082
Simple stones	32 (25.0)	42 (26.1)	47 (21.6)	
Stones with MPD stricture	72 (56.3)	97 (60.2)	150 (68.8)	
Complex lesions	24 (18.8)	22 (13.7)	21 (9.6)	
Location of stones				0.239
Head	100 (78.1)	115 (71.4)	163 (74.8)	
Body/tail	1 (0.8)	2 (1.2)	8 (3.7)	
Mixed	27 (21.1)	44 (27.3)	47 (21.6)	
Complication				
Diabetes mellitus	35 (27.3)	53 (32.9)	52 (23.9)	0.149
Steatorrhea	26 (20.3)	39 (24.2)	47 (21.6)	0.706
Duodenal stenosis	1 (0.8)	0	0	0.227
Pseudocysts	14 (10.9)	17 (10.6)	23 (10.6)	0.993
Biliary stricture	3 (2.3)	2 (1.2)	3 (1.4)	0.720
Portal hypertension	2 (1.6)	3 (1.9)	3 (1.4)	0.932
ESWL sessions, mean (SD)	1.82 (0.99)	1.86 (0.89)	1.83 (0.85)	0.940

*Including hyperlipidemia and trauma.

HCP indicates hereditary CP; ICP, idiopathic CP.

Cannulation and Stone Clearance Rates

Table 2 presents the primary outcomes of the study. Cannulation was successful in 102 patients in group A (79.7%), 140 in group B (87.0%), and 190 in group C (87.2%), and stones were successfully cleared from the MPD in 105 (82.0%), 142 (88.2%), and 193 (88.5%) patients in groups A, B, and C, respectively. There was no statistical difference in the success of MPD cannulation ($P = 0.126$) and stone clearance ($P = 0.184$) with respect to the timing of ERCP after ESWL.

There was no statistical difference in the success rates of MPD cannulation and stone clearance between the 3 groups in the 240 patients who had undergone ERCP before admission ($P > 0.05$ for both). For patients without a prior history of ERCP, the success rates of cannulation ($P = 0.004$) and stone clearance ($P = 0.005$) were significantly higher the longer ERCP was delayed: 71.4% and 76.2% in group A, 81.9% and 85.1% in group B, and 90.9% and 93.6% in group C, respectively. The success rate significantly improved as the interval between ESWL and ERCP increased.

For 2-group comparisons, the success rates of cannulation ($P = 0.001$) and stone clearance ($P = 0.001$) for group C were significantly higher than those for group A. No significant difference in success rates was observed between groups A and B and between groups B and C.

Incidence of PEP and Post-ESWL Complications

Of the 507 enrolled patients, 21 (4.1%) developed PEP, with 7 (5.5%), 5 (3.1%), and 9 (4.1%) patients in groups A, B, and C, respectively. No PEP case was severe, and all patients recovered with conservative treatment. There were no occurrences of perforation, bleeding, or infection. There was no statistically significant difference in the incidence of PEP between the 3 groups or between the patients who did and did not undergo prior ERCP (Table 3).

A total of 932 ESWL sessions were administered to the 507 patients, with 206 (40.6%) having 1 session, 212 (41.8%) having 2 sessions, 66 (13.0%) having 3 sessions, and 23 (4.5%) having 4 or more sessions. Most post-ESWL adverse events were transient, including 33 cases of asymptomatic hyperamylasemia, 2 cases of hematuria, and 3 cases of positive fecal occult blood, all of which resolved spontaneously within 48 hours after ESWL. Post-ESWL complications occurred in 63 cases (12.4%), the most common being acute pancreatitis, all of which were classified as mild. There was no significant difference between the 3 groups with respect to post-ESWL complications (Table 4).

Risk Factors for Primary Outcomes

We performed a risk factor analysis for successful cannulation and successful stone clearance (Table 5). In univariate analysis of successful cannulation, 3 variables, including pancreatic duct morphology, location of stones, and timing of ERCP after ESWL, showed $P < 0.15$. These 3 factors were used to establish a multivariate model. Ultimately, only pancreatic duct morphology was recognized as the risk factor for successful cannulation

TABLE 2. Comparison of the Successful Cannulation and Stone Clearance Rates in Different Groups

Timing of ERCP After ESWL	Successful Cannulation Rate, n (%)	P	Successful Stone Clearance Rate, n (%)	P
Overall		0.126		0.184
<12 h (n = 128)	102 (79.7)		105 (82.0)	
12–36 h (n = 161)	140 (87.0)		142 (88.2)	
>36 h (n = 218)	190 (87.2)		193 (88.5)	
Patients with prior ERCP		0.115		0.208
<12 h (n = 65)	57 (87.7)		57 (87.7)	
12–36 h (n = 67)	63 (94.0)		62 (92.5)	
>36 h (n = 108)	90 (83.3)		90 (83.3)	
Patients without prior ERCP		0.004		0.005
<12 h (n = 63)	45 (71.4)		48 (76.2)	
12–36 h (n = 94)	77 (81.9)		80 (85.1)	
>36 h (n = 110)	100 (90.9)*		103 (93.6)*	

*$P = 0.001$ between groups C and A.

($P < 0.001$). In univariate analysis of successful stone clearance, the same 3 variables, including pancreatic duct morphology, location of stones, and timing of ERCP after ESWL, showed $P < 0.15$. These 3 factors were used to establish a multivariate model. Ultimately, only pancreatic duct morphology was recognized as the risk factor for successful stone clearance ($P < 0.001$).

DISCUSSION

Main pancreatic duct stones may greatly contribute to pain and other symptoms related to pancreatic ductal hypertension; thus, stone removal is the main goal in the treatment of CCP. As it is safe, effective, and minimally invasive, ESWL combined with ERCP has been recommended as first-line therapy for painful uncomplicated CCP with an obstructed MPD in the head and body of the pancreas. Small stones can be removed directly during endoscopic treatment, whereas larger stones need to be fragmented via ESWL before endoscopic extraction.[21,22,42,43] A prior study argued that ESWL alone provided pain relief similar to that of ESWL combined with ERCP in patients with CCP.[44] In clinical practice, ERCP is routinely performed after ESWL as complete stone removal is associated with better abdominal pain relief, but its optimal timing is still a great concern, and studies that focused on the timing of ERCP after ESWL are few. In this retrospective study, we found no significant difference in the success of MPD cannulation and stone clearance in the 507 enrolled patients with respect to the timing of ERCP. Notably, in patients with native papilla and no prior history of ERCP, the success rates of cannulation and stone extraction were significantly higher when ERCP was performed more than 36 hours after ESWL.

TABLE 3. Incidence of PEP With Respect to the Different Intervals Between ERCP and ESWL

Timing of ERCP After ESWL	PEP, n (%)	P
Overall		0.606
<12 h (n = 128)	7 (5.5)	
12–36 h (n = 161)	5 (3.1)	
>36 h (n = 218)	9 (4.1)	
Patients with prior ERCP		0.574
<12 h (n = 65)	2 (3.1)	
12–36 h (n = 67)	4 (6.0)	
>36 h (n = 108)	3 (2.8)	
Patients without prior ERCP		0.082
<12 h (n = 63)	5 (7.9)	
12–36 h (n = 94)	1 (1.1)	
>36 h (n = 110)	6 (5.5)	

TABLE 4. Incidence of Post-ESWL Complications

Timing of ERCP After ESWL	Post-ESWL Complications, n (%)	P
Overall		0.440
<12 h (n = 128)	13 (10.2)	
12–36 h (n = 161)	19 (11.8)	
>36 h (n = 218)	32 (14.7)	
Patients with prior ERCP		0.076
<12 h (n = 65)	4 (6.2)	
12–36 h (n = 67)	13 (19.4)	
>36 h (n = 108)	14 (13.0)	
Patients without prior ERCP		0.084
<12 h (n = 63)	9 (14.3)	
12–36 h (n = 94)	6 (6.4)	
>36 h (n = 110)	18 (16.4)	

A published study claimed that the timing of ERCP after ESWL may be an important factor to the successful clearance of stones from the MPD.[33] Merrill et al[33] retrospectively enrolled 30 patients with CCP and divided them into an early-ERCP group (up to 2 days after ESWL) and a delayed-ERCP group (>2 days after ESWL) and found that the rate of complete MPD clearance was significantly higher in the delayed-ERCP group. However, only patients who had initially undergone unsuccessful ERCP and required subsequent ESWL for stone disintegration were enrolled in the study, and the details about endoscopic intervention before ESWL were not provided. In our study, subgroup analysis found that patients who had ERCP before admission to the hospital had successful cannulation and stone clearance with early ERCP, that is, less than 12 hours after ESWL, a finding different from that of Merrill and colleagues'[33] study. In addition to the timing of ERCP, other studies reported other factors associated with successful endoscopic clearance of stone fragments after ESWL, including the following: there was only 1 stone, the stones were located in the pancreatic head, stone density was less than 820.5 Hounsfield units on a computed tomography scan, and a pancreatic stent had been inserted before ESWL.[20–22] These factors may partly explain the different results among the studies. In multivariate analysis of our study, complex lesion was identified to be the only risk factor for successful cannulation and successful stone clearance. Previous studies demonstrated that failed stone extraction was associated with stones of more than 10 mm and location upstream from a stricture,[45,46] and risk factors for cannulation failure included pancreatic duct strictures and stones.[23,25] Those results were consistent with our findings.

The incidence of post-ESWL complications in the 3 groups was not significantly different in our study. Edema from shock waves in the area of the papilla and pancreatic duct, one of the adverse events of ESWL, can interfere with access to the pancreatic duct and stone removal.[33] In our study, the cannulation of and the stone clearance from the MPD were similarly successful in

TABLE 5. Univariate and Multivariate Analyses of Factors Affecting the Successful Cannulation and Successful Stone Clearance

	Successful Cannulation				Successful Stone Clearance			
	Univariate		Multivariate		Univariate		Multivariate	
Variables	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Sex, female	1.04 (0.60–1.79)	0.902			0.95 (0.54–1.68)	0.853		
Prior ERCP	1.42 (0.86–2.34)	0.169			1.05 (0.63–1.76)	0.851		
Pancreatic duct morphology		<0.001		<0.001		<0.001		<0.001
Simple stones	Reference		Reference		Reference		Reference	
Stones with MPD stricture	0.87 (0.43–1.73)	0.681	0.86 (0.43–1.72)	0.673	0.75 (0.34–1.62)	0.459	0.74 (0.34–1.62)	0.452
Complex lesions	0.16 (0.07–0.35)	<0.001	0.18 (0.08–0.39)	<0.001	0.12 (0.05–0.28)	<0.001	0.13 (0.06–0.31)	<0.001
Location of stones		0.091		0.151		0.103		0.180
Head	Reference		Reference		Reference		Reference	
Body/tail	0.51 (0.13–1.99)	0.334	0.70 (0.16–3.06)	0.637	0.29 (0.08–1.03)	0.056	0.38 (0.09–1.54)	0.173
Mixed	1.88 (0.95–3.69)	0.070	1.66 (0.83–3.35)	0.155	2.02 (0.97–4.22)	0.062	1.77 (0.82–3.80)	0.144
Volume of ESWL	0.97 (0.80–1.17)	0.767			1.04 (0.84–1.27)	0.736		
Timing of ERCP after ESWL		0.081		0.147		0.109		0.223
<12 h	Reference		Reference		Reference		Reference	
12–36 h	1.70 (0.91–3.19)	0.099	1.55 (0.80–3.00)	0.194	1.64 (0.85–3.16)	0.142	1.49 (0.74–3.00)	0.270
>36 h	1.73 (0.96–3.11)	0.067	1.50 (0.80–2.78)	0.203	1.69 (0.92–3.13)	0.094	1.47 (0.76–2.85)	0.254

OR indicates odds ratio; CI, confidence interval.

patients with a history of ERCP, regardless of the timing of ERCP after ESWL, because the effect of edema might have been compensated for by the previous endoscopic intervention, including sphincterotomy and pancreatic stenting.

The risk factors for PEP include female sex, a history of acute pancreatitis or PEP, precut sphincterotomy, and difficult cannulation.[30–32] Papillary and pancreatic edema caused by ESWL increases the difficulty of cannulation in early ERCP, thus increasing the risk of PEP. Therefore, extending the interval between ESWL and ERCP may reduce the risk of PEP. The lack of a significant difference in the occurrence of PEP in the 3 groups of our study may be partly the result of the small sample size; however, delayed ERCP theoretically is preferred because the risk factors for PEP can be complex.

There are some limitations to this study. First, successful cannulation and clearance of MPD stones were considered the primary outcomes. Comparison of clinical success with pain alleviation, the actual purpose of treatment, is also indispensable. With the limited data available, we could not prove that there was a difference in the clinical outcomes of our patients with respect to the timing of ERCP, especially in those with different success rates of cannulation and clearance of MPD. Second, because this was a retrospective study, detailed documentation of prior endoscopic intervention was lacking. Thus, we could not accurately determine the relationship between technical success and prior intervention or even perform a comprehensive analysis of the relationship between the timing of ERCP and post-ERCP complications given the various risk factors. In addition, the range of time between ESWL and ERCP was too broad to pinpoint an ideal interval. The interval between ESWL and ERCP in group A ranged from 30 minutes to 12 hours; thus, it was not possible to accurately determine the "window of time" between the performance of ESWL and the formation of papillary edema.

It has been argued that delaying ERCP after ESWL helps reduce duodenal papillary and pancreatic tissue edema and improves the success of endoscopic stone extraction, while it has also been argued that there is a "window of time" between ESWL and the formation of duodenal papillary edema. However, performing ERCP immediately after ESWL may cause a double attack on the pancreas, increasing post-ERCP complications. Thus, the effect of same-session ESWL and ERCP warrants further validation. In conclusion, the interval between ESWL and ERCP for patients who have undergone ERCP previously does not affect the success rate of cannulation and stone removal from the MPD. However, in patients without prior endoscopic intervention, delaying ERCP may greatly improve the success rate of cannulation and stone removal from the MPD.

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