Digestive and Liver Disease 57 (2025) 417–426

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Liver, Pancreas and Biliary Tract

Safety evaluation of extracorporeal shockwave lithotripsy for pancreatic stones: Experience based on a large chronic pancreatitis cohort

Yu Liu[a,b,c,d,1], Jin-Hui Yi[b,c,1], Peng-Yuan Wang[b,c,e,1], Peng Fu[f,1], Ying Kang[a], Teng Wang[b,c], Di Zhang[b,c], Xi-Hong Zhang[g,h], Jin-Jie Xu[b,c], Song-Lin Zhang[b,c], Pei-Dong Han[b,c], Fan Wang[b,c], Xiao-Yu Zhou[b,c], Jia-Sheng Feng[b,c], Jia-Jun Xu[b,c], Jia-Hao Qian[b,c], Dan Wang[b,c], Hui Chen[b,c], Run-Hui Liu[d,**], Fang-Yu Wang[a,***], Zhao-Shen Li[b,c,*], Liang-Hao Hu[b,c,*]

[a] *Department of Gastroenterology, Jinling Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, 210000, Jiangsu, China*
[b] *Department of Gastroenterology, Changhai Clinical Research Unit, Changhai Hospital; National Key Laboratory of Immunity and Inflammation, Naval Medical University, Shanghai, 200433, China*
[c] *Shanghai Institute of Pancreatic Diseases, Shanghai, 200433, China*
[d] *Department of Pharmacology, College of Pharmacy, Naval Medical University, Shanghai, 200433, China*
[e] *Department of Gastroenterology, the 981st Hospital of PLA, Chengde, 067000, Hebei, China*
[f] *Department of Pharmacy, Changhai Hospital, Naval Medical University, Shanghai, 200433, China*
[g] *Department of Gastroenterology, The Second Hospital of Shandong University, Jinan, 250012, Shandong, China*
[h] *Department of Critical Care Medicine, Liaocheng People's Hospital, Liaocheng, 252000, Shandong, China*

ARTICLE INFO

Article history:
Received 26 April 2024
Accepted 20 August 2024
Available online 11 September 2024

Keywords:
Chronic pancreatitis
Extracorporeal shock wave lithotripsy
Complication
Transient adverse event

ABSTRACT

Background: The safety of extracorporeal shock wave lithotripsy for pancreatic stones (P-ESWL) and adverse events were not evaluated and classified within large sample population. This study aimed to evaluate the safety and classify the adverse events of P-ESWL based on a large sample cohort.
Methods: This is an observational study based on the large prospective chronic pancreatitis (CP) cohort. Patients with painful pancreatic stones over 5 mm who underwent P-ESWL between March 2011 and June 2018 at Shanghai Changhai Hospital were included. Adverse events after P-ESWL including complications and transient adverse events (TAEs) were recorded. Risk factors of adverse events were analyzed through univariable and multivariable logistics regression analysis. Sensitivity analysis was conducted to test the stability of the study.
Results: Totally 2,071 patients underwent 5,002 sessions of P-ESWL were included. The overall complication rate and TAEs rate after all P-ESWL procedures were 5.2% and 20.9%. The complications and TAEs rate decreased obviously within the first 6 sessions. Several independent risk factors for adverse events after P-ESWL were identified. Sensitivity analysis suggested the stability of the results.
Conclusions: P-ESWL is a safe treatment for pancreatic stones. Multiple P-ESWL sessions did not increase the complications and TAEs rate. ClincialTrials.gov number, NCT05916547.

* Corresponding authors at: Department of Gastroenterology, Changhai Clinical Research Unit, Changhai Hospital; National Key Laboratory of Immunity and Inflammation, Naval Medical University, Shanghai Institute of Pancreatic Diseases, 168 Changhai Road, Shanghai, 200433, China.
** Corresponding author at: Department of Pharmacology, College of Pharmacy, Naval Medical University, 800 Xiangyin Road, Shanghai, 200433, China.
*** Corresponding author at: Department of Gastroenterology, Jinling Hospital, Affiliated Hospital of Medical School, Nanjing University, 305 Zhongshan East Road, Nanjing, 210000, Jiangsu, China.
E-mail addresses: lyliurh@126.com (R.-H. Liu), wangfy65@nju.edu.cn (F.-Y. Wang), zhaoshen-li@hotmail.com (Z.-S. Li), lianghao-hu@smmu.edu.cn (L.-H. Hu).
[1] Drs. Liu, Yi, Wang and Fu made equal contributions to this study.

https://doi.org/10.1016/j.dld.2024.08.043
1590-8658/

1. Introduction

Chronic pancreatitis (CP) is a multifactorial chronic inflammatory disease featured with fibrosis and calcification of the pancreas, manifested as abdominal pain, exocrine and endocrine insufficiency. The prevalence rate of CP vary from 36 to 125 per 100,000 population in Japan, China and India [1]. In spite of the low incidence rate, CP-related refractory abdominal pain greatly influences the quality of life for patients, and brings huge economic and medical burden due to the frequent hospitalizations. Pancreatic stones are the typical pathological changes in CP with the prevalence of 75.3% after diagnosis of CP and almost 100% in the longer follow up period [2], leading to obstruction of main pancreatic duct (MPD) and the subsequent pancreatic duct hypertension, which is one of the major causes of refractory abdominal pain. Clearance of pancreatic stones is a therapeutic method for abdominal pain relief.

The conventional treatment strategies for pancreatic stones include extracorporeal shockwave lithotripsy (ESWL), endoscopic treatment and surgery. Due to the minimal invasive feature and repeatability, ESWL and endoscopic retrograde cholangiopancreatography (ERCP) have been the first-line therapy of pancreatic stones in CP patients. There are two types of pancreatic stones according to the physical property, radiopaque and radiolucent stones. According to the 2018 European Society of Gastrointestinal Endoscopy Guideline, radiopaque obstructive MPD stones larger than 5 mm located in the head/body of pancreas should be treated with ESWL, and those are radiolucent or smaller than 5 mm should be treated with ERCP [3]. Since 1987, ESWL has been reported to treat CP patients with pancreatic stones [4]. Several studies have reported the stone clearance rate of ESWL for pancreatic stones (P-ESWL) which proved the efficacy of P-ESWL in treating pancreatic stones [5]. While, researches about the adverse events after P-ESWL were not sufficient and systemical. Different from ERCP with a standard lexicon [6], standard classification of adverse events after P-ESWL was scarce. In our previous research, we tried to come up with a systemical classification for adverse events after P-ESWL [7], while, the study sample was small and the patients' enrollment was restricted in about two years. The adverse events need larger sample study and longer time duration of patients' enrollment to testify.

Based on the aforementioned status quo, we designed an observational study to evaluate the safety and classify adverse events of P-ESWL, as well as explore risk factors for adverse events after P-ESWL based on a larger prospective Changhai CP cohort. Apart from these, we conducted sensitivity analysis to testify the stability of the results.

2. Materials and methods

2.1. Patients and database

The observational study was carried out based on the Changhai CP Database (version number 2.1, Yinma Information Technology Inc., Shanghai, China) (NCT 05916547). Detailed information about Changhai CP Database has been exhibited in previous studies [2,8–11]. From January 2005, data of CP patients who were admitted into Changhai Hospital were collected prospectively. P-ESWL was first carried out in Shanghai Changhai Hospital for hospitalized patients in March 2011. Thus, CP patients who underwent P-ESWL for painful pancreatic stones between March 2011 and June 2018 at Department of Gastroenterology in Shanghai Changhai Hospital were included. Data of these patients were retrospectively analyzed.

Written informed consent was obtained from every patient enrolled in the study. The study was approved by the ethics committee of Shanghai Changhai Hospital on June 18, 2023 (Approved number, CHEC2023-143). The study was registered in 2023 and the ClincialTrials.gov number is NCT05916547.

2.2. Definitions

The diagnosis of CP was based on the Asia-Pacific consensus [12]. Until now, no firm definition of adverse event after P-ESWL has been universally recognized. In this study, we used the previous published definitions for adverse events after P-ESWL [7]. Adverse event of P-ESWL included complications and transient adverse events (TAEs), depending on the severity. Major complications that need specific medical intervention and prolong hospitalization include post-ESWL pancreatitis, bleeding, infection, steinstrasse and perforation. According to the length of hospitalization and the need for invasive treatment, P-ESWL complications were stratified as mild, moderate, and severe complications [7]. Rare complications including intestinal obstruction, splenic rupture and pancreaticobiliary fistula were not exhibited in the classification. Different from the complications, TAEs were mild adverse events which were transient injuries caused by shock waves, requiring no medical intervention. TAEs included skin erythema, mild skin tenderness of the region in contact with the shockwave head, asymptomatic hyperamylasemia (defined as an increase of serum amylase compared with pre-ESWL levels and beyond the upper limit of the normal range without any related symptoms), hematuria, and acute gastrointestinal mucosal injury (manifested as hematemesis and melena).

2.3. Treatment procedure

Patients suffering from painful CP with at least one large pancreatic stone (>5 mm in diameter) in the head/body of pancreas were treated with P-ESWL. P-ESWL was performed by three gastroenterologists using an electromagnetic lithotripter (Compat Delta II; Dornier Med Tech., Wessling, Germany) with bidimensional fluoroscopic targeting facility. Patients with cholangitis due to the common bile duct stricture caused by CP were treated with P-ESWL after the cholangitis been controlled. Patients who were at acute attack of CP were treated with P-ESWL after acute inflammation been completely remission. Patients with pancreatic pseudocyst (PPC) were treated with P-ESWL while a pancreatic surgery team stood by. Patients with palpable masses of PPC underwent transcutaneous drainage pre-ESWL.

Patients underwent repeated P-ESWL sessions on consecutive days until the stones were broken into pieces with diameter less than 3 mm. During the P-ESWL procedures, patients were anesthetized with combination of flurbiprofen and remifentanil through transvenous injection. The shock waves were limited to a maximum of 5000 shocks per session and the intensity was set from 1 to 6 (the majority was 6) with a frequency of 60 to 120 shocks per minute. With these parameters, each P-ESWL session lasted for 60 to 90 min. After the last P-ESWL was finished, patients underwent ERCP in order to remove the stone fragments and treat MPD stricture when necessary. Pancreatic stents were inserted into the MPD when needed according to the guideline [3].

2.4. Statistical analysis

Continuous variables were compared using student's *t*-test or nonparametric Mann-Whitney U test in different groups. Categorical variables were compared using Chi-squared analysis or Fisher's exact test in different groups. Logistic regression model was used to identify the risk factors for complications and TAEs through univariable analysis and multivariable analysis. Odds ratio and the 95% confidence intervals were calculated. A p-value less than 0.05 was considered statistically significant for both the univariable and

Table 1
General characteristics of 2071 patients of CP patients underwent P-ESWL.

Items	Overall (n = 2071)	Male (n = 1485)	Female (n = 586)	P value
Age at the onset of CP, y	37.575 (26.014, 47.542)	39.033 (28.953, 48.660)	30.414 (20.071, 43.656)	<0.001
Age at the diagnosis of CP, y	43.378 (32.222, 52.025)	45.041 (35.677, 53.018)	37.238 (25.545, 48.898)	<0.001
Smoking history[†,‡]	1073 (51.8%)	1061 (71.4%)	12 (2.0%)	<0.001
Alcohol consumption, g/day[†]				<0.001
0	1020 (49.3%)	468 (31.5%)	552 (94.2%)	
0-20	137 (6.6%)	127 (8.6%)	10 (1.7%)	
20-60 (female)/80 (male)	309 (14.9%)	298 (20.1%)	11 (1.9%)	
>60 (female)/80 (male)	605 (29.2%)	592 (39.9%)	13 (2.2%)	
Initial manifestations				0.719
Abdominal pain	1768 (85.4%)	1273 (85.7%)	495 (84.5%)	
Endocrine/Exocrine dysfunction	250 (12.1%)	176 (11.9%)	74 (12.6%)	
Others	53 (2.6%)	36 (2.4%)	17 (2.9%)	
Etiology				<0.001
Alcoholic CP	605 (29.2%)	590 (39.7%)	15 (2.6%)	
Idiopathic CP	1250 (60.4%)	772 (52.0%)	478 (81.6%)	
Others	216 (10.4%)	123 (8.3%)	93 (15.9%)	
Steatorrhea[†]	406 (19.6%)	303 (20.4%)	103 (17.6%)	0.144
DM[†]	502 (24.2%)	366 (24.6%)	136 (23.2%)	0.491
Biliary stricture[†]	97 (4.7%)	80 (5.4%)	17 (2.9%)	0.016
Pancreatic pseudocyst[†]	296 (14.3%)	239 (16.1%)	57 (9.7%)	<0.001
Pancreatic sinistral portal hypertension†	35 (1.7%)	28 (1.9%)	7 (1.2%)	0.272
Type of pain[†]				<0.001
Recurrent acute pancreatitis	715 (34.5%)	557 (37.5%)	158 (27.0%)	
Recurrent pain	710 (34.3%)	448 (30.2%)	262 (44.7%)	
Recurrent acute pancreatitis and pain	564 (27.2%)	415 (27.9%)	149 (25.4%)	
Chronic pain[‖]	82 (4.0%)	65 (4.4%)	17 (2.9%)	
Severe acute pancreatitis[†]	52 (2.5%)	42 (2.8%)	10 (1.7%)	0.142
Successful MPD endoscopic drainage[†]	501 (24.2%)	368 (24.8%)	133 (22.7%)	0.318
Successful MPD surgical drainage[†]	112 (5.4%)	77 (5.2%)	35 (6.0%)	0.475
Main pancreatic duct diameter[¶]	0.800 (0.600, 1.000)	0.800 (0.600, 1.000)	0.800 (0.600, 1.200)	0.002
DM in first-/second-/third-degree relatives	236 (11.4%)	159 (10.7%)	77 (13.1%)	0.117
Pancreatic diseases in first-/second-/third-degree relatives (excluding hereditary CP)	121 (5.8%)	68 (4.6%)	53 (9.0%)	<0.001
Charlson Cormorbidity Index				<0.001
None: CCI score (0)	963 (46.5%)	632 (42.6%)	331 (56.5%)	
Mild: CCI score (1–2)	959 (46.3%)	739 (49.8%)	220 (37.5%)	
Moderate: CCI score (3–4)	144 (7.0%)	112 (7.5%)	32 (5.5%)	
Severe: CCI score (5+)	5 (0.2%)	2 (0.1%)	3 (0.5%)	

CP = chronic pancreatitis, P-ESWL = extracorporeal shockwave lithotripsy for pancreatic stones, DM = diabetes mellitus, MPD = main pancreatic duct, CCI = Charlson Cormorbidity Index.
† Before the performance of the first P-ESWL.
‡ Patients who smoked more than 100 cigarettes were considered as having smoking history.
‖ Patients who have ever experienced chronic pain were classified as chronic pain even though they may experience other pain types during the disease course.
¶ In our study, the main pancreatic duct diameter was obtained for 993 patients, with 711 being male patients and 282 being female patients.

multivariable analysis. Data were analyzed using SPSS 27.0 (SPSS, Chicago, Illinois, USA) and R software (version 4.2.1).

During the risk factors analysis for overall complications after the first P-ESWL (1st-P-ESWL), all complications after 1st-P-ESWL sessions were considered as the study endpoint. During the risk factors analysis for post-ESWL pancreatitis/TAEs after 1st-P-ESWL, post-ESWL pancreatitis/TAEs after 1st-P-ESWL session was considered as the study endpoint. For those patients underwent more than one P-ESWL session, risk factors for adverse events after the subsequent P-ESWL sessions were not analyzed since the subsequent P-ESWL sessions could be influenced by the anterior P-ESWL sessions.

The cohort in this study contained the patients enrolled in the previous research, thus sensitivity analyses in which patients admitted to Changhai hospital between March 2011 and June 2013 reported in the previous study [7] were excluded were conducted to testify the stability of the analysis.

3. Results

3.1. Basic information of patients

A total of 2071 patients underwent 5002 sessions of P-ESWL were included in the study. The mean number of P-ESWL sessions per patient was 2.4 sessions. The general characteristics of patients were listed in Table 1, part of which has been previously disclosed [13] and the parameters associated with P-ESWL procedures were listed in Table 2. There were 93.1% (1929/2071) patients underwent ERCP after P-ESWL. The technological success rate of ERCP was 86.5% (success in stone extraction).

Totally 262 complications and 1047 TAEs occurred in the 5002 P-ESWL procedures for the 2071 patients (Table 3). Most patients only suffered from one type of complications, while four patients suffered from two complications in multiple P-ESWL sessions. One patient suffered from post-ESWL pancreatitis and steinstrasse after the first and the second P-ESWL procedure, separately. One patient suffered from bleeding of the liver and post-ESWL pancreatitis after the first and the eighth P-ESWL procedure, separately. One patient suffered from perforation of the colon after 1st-P-ESWL procedure and intestinal obstruction two days later. The last patient suffered from post-ESWL pancreatitis and infection after the first and the second P-ESWL procedure, separately. Moderate-to-severe complications occurred in a total of 81 procedures. One patient with hepatic subcapsular hematoma underwent percutaneous hematoma drainage. Another patient with perforation of the transverse colon underwent transverse colon repair surgery. All the other patients suffered from complications underwent close observation and conservative treatment and recovered

Table 2
Details of P-ESWL.

Item	Overall (n = 2071)	Male (n = 1485)	Female (n = 586)	P
Age at the first performance of P-ESWL, y	44.937 (33.989, 53.362)	46.748 (37.615, 54.489)	38.095 (27.799, 50.251)	<0.001
Time from onset of CP to P-ESWL, y	4.748 (1.373, 10.315)	4.707 (1.436, 10.263)	4.834 (1.238, 10.427)	0.851
Time from identification of stone(s) to P-ESWL, y				0.489
0–1	1452 (70.1%)	1045 (70.4%)	407 (69.5%)	
1–3	298 (14.4%)	215 (14.5%)	83 (14.2%)	
3–5	132 (6.4%)	87 (5.9%)	45 (7.7%)	
>5	189 (9.1%)	138 (9.3%)	51 (8.7%)	
Number of P-ESWL sessions	2 (1, 3)	2 (1, 3)	2 (1, 3)	0.072
Prophylactic rectal indometacin	307 (14.8%)	222 (14.9%)	85 (14.5%)	0.837
Location of stone(s)				0.433
Head	1453 (70.2%)	1046 (70.4%)	407 (69.5%)	
Body/tail	47 (2.3%)	37 (2.5%)	10 (1.7%)	
Head and at least another location	571 (27.6%)	402 (27.1%)	169 (28.8%)	
Radiological finding of targeted stone(s)				0.048
Radiopaque	2050 (99.0%)	1475 (99.3%)	575 (98.1%)	
Radiolucent	4 (0.2%)	2 (0.1%)	2 (0.3%)	
Mixed	17 (0.8%)	8 (0.5%)	9 (1.5%)	
Diameter of the largest stone(s), cm				<0.001
0.5–1	972 (46.9%)	734 (49.4%)	238 (40.6%)	
1–2	766 (37.0%)	537 (36.2%)	229 (39.1%)	
>2	333 (16.1%)	214 (14.4%)	119 (20.3%)	
Exposure time of X-ray in P-ESWL, min				0.416
0–5	1302 (62.9%)	928 (62.5%)	374 (63.8%)	
5–10	732 (35.3%)	527 (35.5%)	205 (35.0%)	
>10	37 (1.8%)	30 (2.0%)	7 (1.2%)	

P-ESWL = extracorporeal shockwave lithotripsy for pancreatic stones, CP = chronic pancreatitis.

Table 3
The frequency and severity of adverse events after P-ESWL.

Adverse events	Overall P-ESWL sessions (n = 5002)	First P-ESWL session (n = 2071)	Subsequent P-ESWL sessions (n = 2931)	P value
Overall complications	262 (5.2%)	193 (9.3%)	69 (2.4%)	<0.001
Post-ESWL pancreatitis	216 (4.3%)	160 (7.7%)	56 (1.9%)	<0.001
Mild	149 (68.9%)	106 (66.3%)	43 (76.8%)	0.308*
Moderate	62 (28.7%)	50 (31.3%)	12 (21.4%)	
Severe	5 (2.3%)	4 (2.5%)	1 (1.8%)	
Infection	25 (0.50)	19 (0.92)	6 (0.20%)	<0.001
Mild	21 (84.0%)	16 (84.2%)	5 (83.3%)	1.000*
Moderate	4 (16.0%)	3 (15.8%)	1 (16.7%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Bleeding	7 (0.1%)	5 (0.2%)	2 (0.1%)	0.134
Mild	4 (57.1%)	2 (40.0%)	2 (100.0%)	1.000*
Moderate	3 (42.9%)	3 (60.0%)	0 (0.0%)	
Severe	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Perforation	4 (0.1%)	3 (0.1%)	1 (0.0%)	0.313
Mild	2 (50.0%)	1 (33.3%)	1 (100.0%)	0.429*
Moderate	1 (25.0%)	1 (33.3%)	0 (0.0%)	
Severe	1 (25.0%)	1 (33.3%)	0 (0.0%)	
Steinstrasse	8 (0.2%)	5 (0.2%)	3 (0.1%)	0.288
Mild	5 (62.5%)	3 (60.0%)	2 (66.7%)	1.000*
Moderate	2 (25.0%)	1 (20.0%)	1 (33.3%)	
Severe	1 (12.5%)	1 (20.0%)	0 (0.0%)	
Overall TAEs	1047 (20.9%)	547 (26.4%)	500 (17.1%)	<0.001
Asymptomatic hyperamylasemia	933 (18.7%)	499 (24.1%)	434 (14.8%)	<0.001
Hematuria	61 (1.2%)	26 (1.3%)	35 (1.2%)	0.846
Acute gastrointestinal mucosal injury†	53 (1.1%)	22 (1.1%)	31 (1.1%)	0.987

P-ESWL = extracorporeal shockwave lithotripsy for pancreatic stones, ESWL = extracorporeal shockwave lithotripsy, TAEs = Transient adverse events. (One patient with intestinal obstruction (severe) and one with pancreaticobiliary fistula (moderate) were not exhibited in the table.)

* The P value represents the comparison of severity of complications after the first P-ESWL and subsequent P-ESWL sessions.

† Acute gastrointestinal mucosal injury was manifested as hematemesis and melena.

well. In general, the P-ESWL complication rate was 5.2% and the moderate-to-severe complication rate was 1.6% for the total 5002 P-ESWL procedures. The complication rate was higher after 1st-P-ESWL procedure, with the total complication rate of 9.3% and the post-ESWL pancreatitis rate of 7.7%. The overall TAEs rate after P-ESWL was 20.9% (1047/5002) in which asymptomatic hyperamylasemia was the most common TAE with the rate of 18.7% (933/5002).

3.2. Complications and TAEs in multiple P-ESWL sessions

As the number of P-ESWL sessions increased, the complications and TAEs rate decreased within the first 6 sessions which accounted for about 98% (4890/5002) P-ESWL sessions (Fig. 1, Supplementary Table 1). Fcor 63 and 28 patients underwent 7 and 8 P-ESWL sessions, post-ESWL pancreatitis occurred in 1 and 2 patients after the seventh and eighth P-ESWL procedure, respectively,

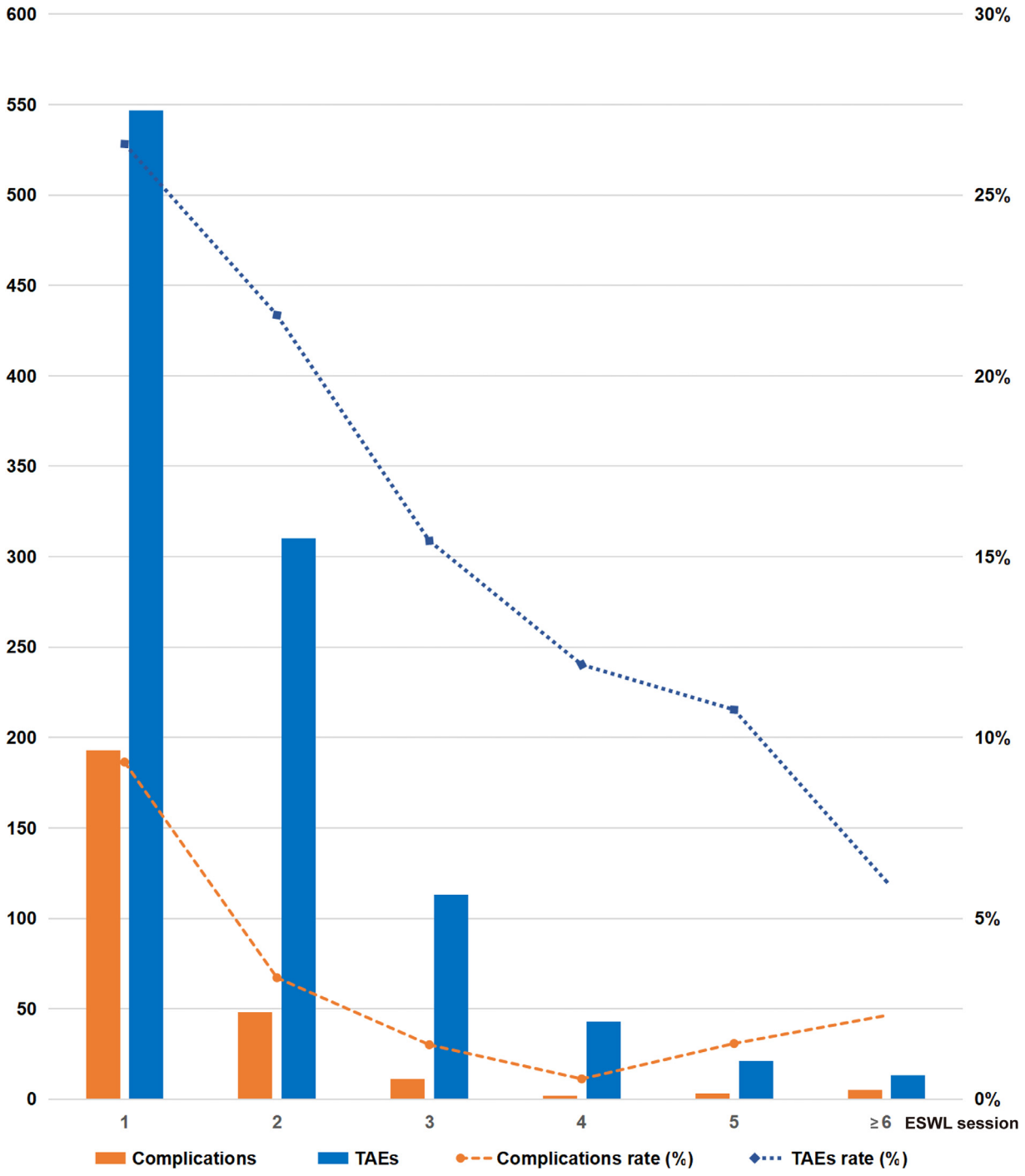

Fig. 1. The number and rate of complications and TAEs in patients underwent different P-ESWL sessions. The left vertical coordinate shows the number of patients suffered from complications and TAEs in those underwent different P-ESWL sessions. The right vertical coordinate shows the complication rate and TAEs rate in different number of P-ESWL sessions. P-ESWL = extracorporeal shockwave lithotripsy for pancreatic stones, TAEs = transient adverse events.

which led to the increase of the complication rate. When comparing the complications after 1st-P-ESWL session and the subsequent P-ESWL sessions, subsequent P-ESWL sessions showed lower incidence of overall complications, post-ESWL pancreatitis and infection. No significant difference was observed between incidence of complications or severity of complications after 1st-P-ESWL session and subsequent P-ESWL sessions (Table 3). Similarly, the rate of asymptomatic hyperamylasemia was higher in 1st-P-ESWL session than the subsequent P-ESWL sessions and there was no difference in incidence of hematuria and acute gastrointestinal mucosal injury between 1st-P-ESWL and subsequent P-ESWL sessions (Table 3).

3.3. Risk factors analysis for overall complications after 1st-P-ESWL

All potential risk factors were included in the univariable analysis. Totally 14 factors were associated with the overall complications after 1st-P-ESWL significantly through univariable analysis and were enrolled in the multivariable analysis. Finally, four independent risk factors were identified as risk factors, including fe-

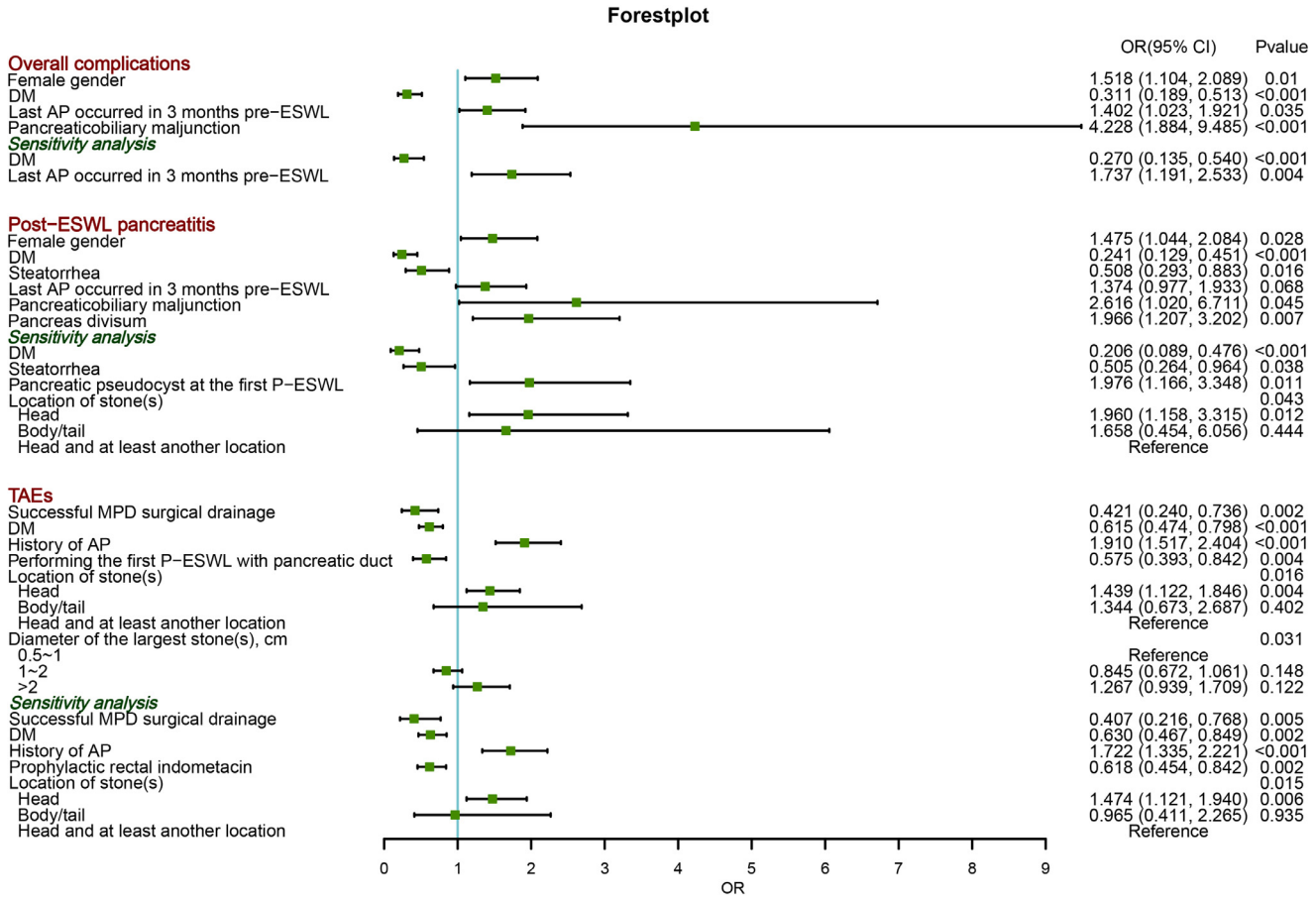

Fig. 2. The forestplot of independent risk factors for overall complications, post-ESWL pancreatitis and TAEs after the first P-ESWLs and the corresponding sensitivity analysis. AP = acute pancreatitis, DM = diabetes mellitus, MPD = main pancreatic duct, P-ESWL = extracorporeal shockwave lithotripsy for pancreatic stones; TAEs = transient adverse events

male gender, diabetes mellitus (DM) pre-ESWL, AP occurred within 3 months pre-ESWL and pancreaticobiliary maljunction (Fig. 2, Table 4 and Supplementary Table 2).

3.4. Risk factors analysis for post-ESWL complications after 1st-P-ESWL

Totally 160 patients suffered from post-ESWL pancreatitis after 1st-P-ESWL procedure, most of them were mild post-ESWL pancreatitis. In total, 13 factors were identified as risk factors for post-ESWL pancreatitis after 1st-P-ESWL procedure. Finally, 6 factors were identified as independent risk factors, including female gender, DM pre-ESWL, steatorrhea pre-ESWL, AP occurred within 3 months pre-ESWL, pancreaticobiliary maljunction and pancreas divisum (Fig. 2, Table 4 and Supplementary Table 3).

There were 19 patients suffered from infection after 1st-P-ESWL procedure. Univariable and multivariable Logistics regression analyses showed successful MPD surgical drainage and pancreaticobiliary maljunction were risk factors for infection after P-ESWL (Supplementary Table 4). Five patients had bleeding after 1st-P-ESWL procedure and the Logistics regression analyses showed severe acute pancreatitis history and pancreatic diseases in first-/second-/third-degree relatives (excluding hereditary CP) were risk factors for bleeding after P-ESWL (Supplementary Table 5). Three patients had perforation after 1st-P-ESWL procedure and the Logistics regression analyses showed multiple stones were protective factor for perforation after P-ESWL (Supplementary Table 6). Five patients suffered from steinstrasse after 1st-P-ESWL procedure and the univariable Logistics regression analyses showed steatorrhea pre-ESWL and pancreatic diseases in first-/second-/third-degree relatives (excluding hereditary CP) were risk factors for steinstrasse after P-ESWL (Supplementary Table 7). While, only pancreatic diseases in first-/second-/third-degree relatives (excluding hereditary CP) was identified as significant risk factor for steinstrasse after P-ESWL in multivariable analyses (Supplementary Table 7).

3.5. Risk factors analysis for TAEs after 1st-P-ESWL

There were 547 TAEs after the 2071 P-ESWL procedures. In the univariable analysis, 13 factors were defined as risk factors for TAEs after 1st-P-ESWL and were included in the multivariable analysis. And finally, 6 independent risk factors for TAEs after 1st-P-ESWL were identified including successful MPD surgical drainage, DM pre-ESWL, history of AP pre-ESWL, performing 1st-P-ESWL with pancreatic duct, location of stones and diameter of the largest stones (Fig. 2, Table 4 and Supplementary Table 8).

3.6. Sensitivity analysis

After excluding 634 patients enrolled in the previous study, a series of sensitivity analysis were conducted. The total complications and TAEs rate were 4.6% and 21.7%, respectively. The complications and TAEs rate decreased within the first 6 sessions which accounted for about 98% (3464/3532) P-ESWL sessions as the number of P-ESWL sessions increased (Supplementary Figure 1, Supplementary Table 1). The Sensitivity analysis showed DM pre-ESWL and AP occurred within 3 months pre-ESWL were risk factors for

Table 4
Risk factors analysis and sensitivity analysis for adverse events in CP patients after the first P-ESWL.

Predictive factors for overall complications in CP patients after the first P-ESWL					
Predictors	n (%)	Univariate Analysis		Multivariate Analysis	
		P	OR (95% CI)	P	OR (95% CI)
Female gender	586 (28.3)	0.010	1.504 (1.101, 2.056)	0.010	1.518 (1.104, 2.089)
DM†	502 (24.2)	<0.001	0.302 (0.184, 0.496)	<0.001	0.311 (0.189, 0.513)
AP occurred within 3 months pre-ESWL†	639 (30.9)	0.018	1.450 (1.065, 1.973)	0.035	1.402 (1.023, 1.921)
Pancreaticobiliary maljunction	32 (1.5)	<0.001	4.017 (1.831, 8.812)	<0.001	4.228 (1.884, 9.485)
Sensitivity analysis					
DM†	325 (22.6)	<0.001	0.252 (0.126, 0.502)	<0.001	0.270 (0.135, 0.540)
AP occurred within 3 months pre-ESWL†	474 (33.0)	<0.001	1.888 (1.299, 2.745)	0.004	1.737 (1.191, 2.533)
Predictive factors for post-ESWL pancreatitis in CP patients after the first P-ESWL					
Predictors	n (%)	Univariate Analysis		Multivariate Analysis	
		P	OR (95% CI)	P	OR (95% CI)
Female gender	586 (28.3)	0.013	1.534 (1.096, 2.148)	0.028	1.475 (1.044, 2.084)
DM†	502 (24.2)	<0.001	0.214 (0.115, 0.397)	<0.001	0.241 (0.129, 0.451)
Steatorrhea†	406 (19.6)	0.001	0.402 (0.234, 0.692)	0.016	0.508 (0.293, 0.883)
AP occurred within 3 months pre-ESWL	639 (30.9)	0.016	1.505 (1.080, 2.098)	0.068	1.374 (0.977, 1.933)
Pancreaticobiliary maljunction	32 (1.5)	0.024	2.825 (1.145, 6.967)	0.045	2.616 (1.020, 6.711)
Pancreas divisum	165 (8.0)	0.002	2.091 (1.302, 3.358)	0.007	1.966 (1.207, 3.202)
Sensitivity analysis					
DM†	325 (22.6)	<0.001	0.177 (0.077, 0.406)	<0.001	0.206 (0.089, 0.476)
Steatorrhea†	271 (18.9)	0.012	0.441 (0.233, 0.834)	0.038	0.505 (0.264, 0.964)
Pancreatic pseudocyst at the first P-ESWL	155 (10.8)	0.015	1.894 (1.132, 3.169)	0.011	1.976 (1.166, 3.348)
Location of stone(s)		0.010		0.043	
Head	995 (69.2)	0.003	2.224 (1.324, 3.737)	0.012	1.960 (1.158, 3.315)
Body/tail	31 (2.2)	0.193	2.339 (0.650, 8.422)	0.444	1.658 (0.454, 6.056)
Head and at least another location	411 (28.6)	Reference		Reference	
Predictive factors for post-ESWL TAEs in CP patients after the first P-ESWL					
Predictors	n (%)	Univariate Analysis		Multivariate Analysis	
		P	HR (95% CI)	P	HR (95% CI)
Successful MPD surgical drainage†	112 (5.4)	0.003	0.430 (0.247, 0.748)	0.002	0.421 (0.240, 0.736)
DM†	502 (24.2)	<0.001	0.555 (0.431, 0.715)	<0.001	0.615 (0.474, 0.798)
History of AP†	1316 (63.5)	0.036	1.991 (1.598, 2.482)	<0.001	1.910 (1.517, 2.404)
Performing the first P-ESWL with pancreatic duct	204 (9.9)	0.006	0.591 (0.406, 0.859)	0.004	0.575 (0.393, 0.842)
Location of stone(s)		<0.001		0.016	
Head	1453 (70.2)	<0.001	1.672 (1.318, 2.121)	0.004	1.439 (1.122, 1.846)
Body/tail	47 (2.3)	0.159	1.621 (0.827, 3.174)	0.402	1.344 (0.673, 2.687)
Head and at least another location	571 (27.6)	Reference		Reference	
Diameter of the largest stone(s), cm		0.031		0.031	
0.5–1	972 (46.9)	Reference		Reference	
1–2	766 (37.0)	0.010	0.749 (0.601, 0.933)	0.148	0.845 (0.672, 1.061)
>2	333 (16.1)	0.764	0.958 (0.724, 1.267)	0.122	1.267 (0.939, 1.709)
Sensitivity analysis					
Successful MPD surgical drainage†	77 (5.4)	0.006	0.415 (0.222, 0.776)	0.005	0.407 (0.216, 0.768)
DM†	325 (22.6)	<0.001	0.584 (0.436, 0.782)	0.002	0.630 (0.467, 0.849)
History of AP†	923 (64.2)	<0.001	1.835 (1.432, 2.353)	<0.001	1.722 (1.335, 2.221)
Prophylactic rectal indometacin†	283 (19.7)	0.003	0.627 (0.462, 0.850)	0.002	0.618 (0.454, 0.842)
Location of stone(s)	<0.001			0.015	
Head	995 (69.2)	<0.001	1.697 (1.300, 2.214)	0.006	1.474 (1.121, 1.940)
Body/tail	31 (2.2)	0.685	1.189 (0.515, 2.747)	0.935	0.965 (0.411, 2.265)
Head and at least another location	411 (28.6)	Reference		Reference	

CP = chronic pancreatitis, P-ESWL = extracorporeal shockwave lithotripsy for pancreatic stones, EWSL = extracorporeal shockwave lithotripsy, AP = acute pancreatitis, DM = diabetes mellitus, MPD = main pancreatic duct, OR = odds ratio, CI = confidence interval ESWL.
† Before the performance of the first P-ESWL.

overall complications after 1st-P-ESWL (Fig. 2, Table 4 and Supplementary Table 9). For post-ESWL pancreatitis after 1st-P-ESWL, sensitivity analysis showed DM pre-ESWL, steatorrhea pre-ESWL, pancreatic pseudosyst at the first P-ESWL and location of stones were risk factors (Fig. 2, Table 4 and Supplementary Table 10). Sensitivity analysis showed successful MPD surgical drainage, DM pre-ESWL, history of AP pre-ESWL, prophylactic rectal indometacin pre-ESWL and location of stones were risk factors for TAEs after 1st-P-ESWL (Fig. 2, Table 4 and Supplementary Table 11).

4. Discussion

Although P-ESWL has been proved to be a safe minimal invasive procedure for pancreatic stones larger than 5 mm since it was first applied in pancreatic stones in 1987, complications and TAEs occasionally emerged and were reported. In this research, the overall complication rate was 5.2%, in which post-ESWL pancreatitis was the major complication type with the rate of 4.3%, and the rate of TAEs was 20.9%. The complication rate was higher after 1st-P-ESWL procedure with the rate of 9.3% compared with the subsequent P-ESWL sessions and the rate of TAEs after 1st-P-ESWL procedure was 26.4%. Post-ESWL pancreatitis was also the major type of complications after 1st-P-ESWL procedure with the rate of 7.7%.

As the number of P-ESWL sessions increased, the complications and TAEs rate showed a gradually decreasing trend in general, especially in the first 6 sessions which accounted for about 98% P-ESWL sessions. According to Fig. 1, there seemed to be an increase trend of complication rate after the sixth P-ESWL session. This is due to the relatively small number of patients underwent more than 6 sessions of P-ESWL procedures. Thus, even one or two complications would result in a high rate of complications. In addition, the incidence of overall complications and overall TAEs was lower in subsequent P-ESWL sessions compared with the first P-ESWL session. These results reflect multiple P-ESWL sessions did not increase the incidence of complications and TAEs. From this perspective, the number of P-ESWL sessions could be determined based on the therapeutic goal, without worrying about whether multiple P-ESWL procedures would increase the occurrence of complications.

Through univariable and multivariable Logistics analysis, several risk factors were identified as predictors for complications and TAEs after P-ESWL procedures. DM pre-ESWL, which represented pancreatic endocrine insufficiency, was the common independent protective factor for overall complications after 1st-P-ESWL procedure, post-ESWL pancreatitis after 1st-P-ESWL procedure, and TAEs after 1st-P-ESWL procedure. The result was consistent between the total analysis and sensitivity analysis. This may be caused by the deterioration of pancreatic function suggested the late phase of CP. Hence, complications like post-ESWL pancreatitis related to the function of pancreas were less in patients with pre-ESWL diabetes compared with those without diabetes. The other aspect of pancreatic function, steatorrhea, which represents the severe form of pancreatic exocrine insufficiency, was identified as the independent protective factor for post-ESWL pancreatitis after 1st-P-ESWL procedure. The results were quite consistent with sensitivity analysis and the previous studies of our center [7]. While, steatorrhea was not identified as a protective factor for overall complications and TAEs. In addition, steatorrhea was not selected out in these sensitivity analysis. The possible reason may be the low detection rate of pancreatic exocrine insufficiency in our country five years ago. The diagnosis of steatorrhea was mainly based on the symptoms, thus some patients with steatorrhea were underdiagnosed. Fecal elastase test is being carried on in our hospital nowadays and the pancreatic exocrine function may be evaluated better and the study may be more accurate with the new results in the future.

Pancreas divisum and pancreaticobiliary maljunction were also identified as common risk factors for complications, especially for post-ESWL pancreatitis. This was also in line with the previous studies [7]. The special anatomy of pancreas divisum and pancreaticobiliary maljunction caused difficulty of drainage of pancreatic fluid, which resulted in higher possibility of pancreatitis [14–19]. Moreover, the fragmented pancreatic stones further increased the difficulty of pancreatic fluid drainage. Thus, complications such as post-ESWL pancreatitis were more likely to occur in patients with such anatomical abnormality.

Prophylactic rectal indomethacin was considered to reduce the risk of post-ESWL pancreatitis. 14.8% of our patients were enrolled in the clinical trial of prophylactic rectal indomethacin [20]. While, in the current study, prophylactic rectal indomethacin was identified as protective factor for TAEs after 1st-P-ESWL only in the sensitivity analysis but not in other analysis. This may be due to the relatively small sample size of patients accepted prophylactic rectal indomethacin in our study.

Some risk factors were not identified as risk factors in sensitivity analysis. This may be due the maturing technical skills of P-ESWLs. The previous study enrolled patients from March 2011 to June 2013 when P-ESWL was first applied in our hospital as a new technique. With time going on, patients with some risk factors were less likely to suffer from post-ESWL complications due to the technical skills developing and the operating experience accumulating. From this perspective, the results of the current study were quite robust and reasonable.

Except for the common complications during the 5002 P-ESWL procedures, some rare complications also appeared. In our study, one patient suffered from intestinal obstruction after P-ESWL, and another patient suffered from pancreaticobiliary fistula. Some other rare complications by P-ESWL have also been reported, such as renovascular acute renal failure [21], lung contusion [22], colonic hematoma [23], transient intussusception [24], mesenteric hematoma [25], hepatic subcapsular hematoma [26,27], hemorrhagic pseudoaneurysms in a pancreatic pseudocyst [28], splenic abscess [29], etc. Skin erythema and tenderness were seen in most patients and brought little influence; thus, they were not listed out or analyzed as a TAE in this study.

The technical success defined by success in stone extraction was 86.5% which was similar to studies reported by our team previously [30,31,32]. There are also some other cohort studies reported similar results. The complete stone clearance reported by Tandan et al. was 72.6% (3722/5124) [33]. Yamamoto S. et al. reported the overall stone clearance was 79% in their study [34]. Bick B.L. et al. reported 86.7% of the patients had success in stone clearance [35]. Several randomized controlled trials (RCTs) also reported similar efficacy. Cahen et al. reported that complete stone extraction was accomplished in 89% patients [36]. Issa et al. reported complete ductal clearance was 62% in endoscopically treatment group [37]. In Talukdar et al's study, 88% patients had complete pancreatic ductal clearance [38]. Hence, the efficacy of P-ESWL and ERCP reflected by stone clearance rate in our study was similar to other studies including the RCTs. For patients with failed stone clearance, surgery is an option for further treatment as it is recommended by several guidelines [39,40]. Surgical intervention is effective in carefully selected patients, such as patients with poorly controlled pain, duodenal, biliary and pancreatic duct obstruction, and suspicion of cancer. Some RCTs reported the efficacy of surgery in comparison of endoscopic treatment [36,37]. Though P-ESWL and endoscopic treatment is considered as first-line treatment in traditional view due to the invasiveness and low complication rate, surgery first may be a new option for some patients in the future [39,40].

There were some limitations in the study. First, not all potential risk factors were enrolled in the risk factor analysis, yet we

have tried our best to include all the important indicators. Especially, the data of MPD diameter was incomplete. Among the 2071 patients included in our study, the MPD diameter was measured for 993 patients (711 male and 282 female). For the 1078 patients, the MPD dimeter was not evaluated and thus not reported. Due to the incompletion of the data and the complexity of main pancreatic duct morphology, it was not suitable for the risk factor analysis. Second, the population in this study were all from the single center where the gastroenterologists were all quite experienced in performing P-ESWL and ERCP procedures. Thus, the complication rate could not adequately represent other hospitals in China. Third, we did not do the subgroup analysis of patients with different age or comorbidities. While, the Logistic regression analysis revealed the age and comorbidity index were not risk factors for complications after P-ESWL.

In conclusion, P-ESWL is a safe minimal invasive treatment for pancreatic stones in painful CP patients. Post-ESWL pancreatitis is the most common complication after P-ESWL. The complications and TAEs rate decreased with the increase of P-ESWL sessions. Multiple P-ESWL sessions did not increase the complications and TAEs rate.

Authorship statement

Dr. Hu is the guarantor of the article.

Dr. Liu, Yi, Wang, and Fu: contributed to the conception and design; analysis and interpretation of the data; drafting of the article; final approval of the article.

Dr. Kang, Wang, Zhang, Zhang, Xu, Zhang, Han, Wang, Zhou, Feng, Xu, Qian, Chen, and Wang: contributed to the analysis and interpretation of the data; final approval of the article.

Dr. Liu, Wang, Li and Hu: contributed to the conception and design; critical revision of the article for important intellectual content; final approval of the article.

All authors approved the final version of the article, including the authorship list.

Data transparency statement

Data would be available to other researchers upon reasonable request from the corresponding author.

Funding

This study was supported by the National Natural Science Foundation of China [Grant No. 82200723(Liu Y), 82270679(Hu LH), 82104257(Wang PY)], China Postdoctoral Science Foundation [Grant No. 2023M734266(Liu Y)], the Science and Technology Commission of Shanghai Municipality [No. 20ZR1456400(Fu P)], the Programs of Shanghai Municipal Government [No. SHDC12021107(Li ZS)]

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgments

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dld.2024.08.043.

References

[1] Singh VK, Yadav D, Garg PK. Diagnosis and management of chronic pancreatitis: a review. JAMA 2019;322:2422–34. doi:10.1001/jama.2019.19411.
[2] Hao L, Liu Y, Xie T, et al. Risk factors and nomogram for pancreatic stone formation in chronic pancreatitis over a long-term course: a cohort of 2,153 patients. Digestion 2020;101:473–83. doi:10.1159/000500941.
[3] Dumonceau JM, Delhaye M, Tringali A, et al. Endoscopic treatment of chronic pancreatitis: european Society of Gastrointestinal Endoscopy (ESGE) Guideline - Updated August 2018. Endoscopy 2019;51:179–93. doi:10.1055/a-0822-0832.
[4] Sauerbruch T, Holl J, Sackmann M, et al. Disintegration of a pancreatic duct stone with extracorporeal shock waves in a patient with chronic pancreatitis. Endoscopy 1987;19:207–8. doi:10.1055/s-2007-1018284.
[5] Gnecco J, Brown LK, Boregowda U, et al. Pancreatic Stones and Extracorporeal Shockwave Lithotripsy: a Review of the Literature. Pancreas 2022;51:916–22. doi:10.1097/mpa.0000000000002129.
[6] Cotton PB, Eisen GM, Aabakken L, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010;71:446–54. doi:10.1016/j.gie.2009.10.027.
[7] Li BR, Liao Z, Du TT, et al. Risk factors for complications of pancreatic extracorporeal shock wave lithotripsy. Endoscopy 2014;46:1092–100. doi:10.1055/s-0034-1377753.
[8] Hao L, Liu Y, Wang T, et al. Extracorporeal shock wave lithotripsy is safe and effective for geriatric patients with chronic pancreatitis. J Gastroenterol Hepatol 2019;34:466–73. doi:10.1111/jgh.14569.
[9] Liu Y, Wang D, Guo HL, et al. Risk factors and nomogram for diabetes mellitus in idiopathic chronic pancreatitis. J Gastroenterol Hepatol 2020;35:343–52. doi:10.1111/jgh.14785.
[10] Liu Y, Wang D, Hao L, et al. Risk factors analysis and nomogram development for pancreatic pseudocyst in idiopathic chronic pancreatitis. Pancreas 2020;49:967–74. doi:10.1097/mpa.0000000000001610.
[11] Liu Y, Yin XY, Wang D, et al. Risk factor analysis and nomogram development for steatorrhea in idiopathic chronic pancreatitis. J Dig Dis 2022;23:331–40. doi:10.1111/1751-2980.13102.
[12] Tandon RK, Sato N, Garg PK. Chronic pancreatitis: asia-Pacific consensus report. J Gastroenterol Hepatol 2002;17:508–18. doi:10.1046/j.1440-1746.2002.02762.x.
[13] Liu Y, Yin XY, Cui JH, et al. Long-term clinical outcomes of extracorporeal shockwave lithotripsy and endoscopic retrograde cholangiopancreatography for pancreatic duct stone treatment in patients with chronic pancreatitis. Aliment Pharmacol Ther 2024;21. doi:10.1111/apt.18224.
[14] Kamisawa T, Takuma K, Anjiki H, et al. Pancreaticobiliary maljunction. Clinical gastroenterology and hepatology: the official clinical practice journal of the. Am Gastroenterol Assoc 2009;7:S84–8. doi:10.1016/j.cgh.2009.08.024.
[15] Zhang JY, Deng ZH, Gong B. Clinical characteristics and endoscopic treatment of pancreatitis caused by pancreaticobiliary malformation in Chinese children. J Dig Dis 2022;23:651–9. doi:10.1111/1751-2980.13152.
[16] Covantev S. Pancreas divisum: a reemerging risk factor for pancreatic diseases. Rom J Intern Med 2018;56:233–42. doi:10.2478/rjim-2018-0022.
[17] Adike A, El Kurdi BI, Gaddam S, et al. Pancreatitis in patients with pancreas divisum. Pancreas 2017;46:e80–1. doi:10.1097/mpa.0000000000000938.
[18] Lin TK, Abu-El-Haija M, Nathan JD, et al. Pancreas divisum in pediatric acute recurrent and chronic pancreatitis: report from INSPPIRE. J Clin Gastroenterol 2019;53:e232–8. doi:10.1097/mcg.0000000000001063.
[19] Wood CG, Lopes Vendrami C, Craig E, et al. Pancreatitis in the developmentally anomalous pancreas. Abdominal Radiol. 2020;45:1316–23. doi:10.1007/s00261-019-02197-8.
[20] Qian YY, Ru N, Chen H, et al. Rectal indometacin to prevent pancreatitis after extracorporeal shock wave lithotripsy (RIPEP): a single-centre, double-blind, randomised, placebo-controlled trial. Lancet Gastroenterol Hepatol 2022;7:238–44. doi:10.1016/s2468-1253(21)00434-9.
[21] Cecere N, Goffette P, Deprez P, et al. Renovascular acute renal failure precipitated by extracorporeal shock wave lithotripsy for pancreatic stones. Clin Kidney J 2015;8:426–9. doi:10.1093/ckj/sfv031.
[22] Yi JH, Wang D, Chen H, et al. Lung contusion after extracorporeal shock wave lithotripsy for pancreatic stones: a case report. Medicine 2022;101:e30063. doi:10.1097/md.0000000000030063.
[23] Liu Y, Hao L, Wang T, et al. Colonic hematoma after extracorporeal shock wave lithotripsy for pancreatic stones: a case report. BMC Gastroenterol 2019;19:208. doi:10.1186/s12876-019-1117-7.
[24] Ma JY, Pan P, He ZX, et al. A rare complication of ESWL for pancreatic stones. Am J Gastroenterol 2022;117:1030. doi:10.14309/ajg.0000000000001737.
[25] Liu Y, Hao L, Wang LS, et al. Large mesenteric hematoma after extracorporeal shock wave lithotripsy for pancreatic stones: a case report. Medicine 2018;97:e13114. doi:10.1097/md.0000000000013114.
[26] Bi YW, Wang D, Du TT, et al. Hepatic subcapsular hematoma breaking into the abdominal cavity after extracorporeal shock wave lithotripsy for pancreatic stones. J Dig Dis 2018;19:314–17. doi:10.1111/1751-2980.12510.
[27] Hirata N, Kushida Y, Ohguri T, et al. Hepatic subcapsular hematoma after extracorporeal shock wave lithotripsy (ESWL) for pancreatic stones. J Gastroenterol 1999;34:713–16. doi:10.1007/s005350050325.
[28] Nakagawa Y, Abe T, Uchida M, et al. Hemorrhagic pseudoaneurysm in a pancreatic pseudocyst after extracorporeal shock wave lithotripsy for pancreatolithiasis. Endoscopy 2011;43(Suppl 2):E310–11 UCTN. doi:10.1055/s-0030-1256642.

[29] Plaisier PW, den Hoed PT. Splenic abscess after lithotripsy of pancreatic duct stones. Dig Surg 2001;18:231–2. doi:10.1159/000050140.
[30] Li BR, Liao Z, Du TT, et al. Extracorporeal shock wave lithotripsy is a safe and effective treatment for pancreatic stones coexisting with pancreatic pseudocysts. Gastrointest Endosc 2016;84:69–78. doi:10.1016/j.gie.2015.10.026.
[31] Hu LH, Ye B, Yang YG, et al. Extracorporeal shock wave lithotripsy for Chinese patients with pancreatic stones: a prospective study of 214 cases. Pancreas 2016;45:298–305. doi:10.1097/mpa.0000000000000464.
[32] Wang D, Bi YW, Ji JT, et al. Extracorporeal shock wave lithotripsy is safe and effective for pediatric patients with chronic pancreatitis. Endoscopy 2017;49:447–55. doi:10.1055/s-0043-104527.
[33] Tandan M, Nageshwar Reddy D, Talukdar R, et al. ESWL for large pancreatic calculi: report of over 5000 patients. Pancreatology 2019;19:916–21. doi:10.1016/j.pan.2019.08.001.
[34] Yamamoto S, Inui K, Katano Y, et al. Pancreatic stones: clinical outcomes with nonsurgical treatment in a japanese single-center study. Pancreas 2022;51:205–11. doi:10.1097/mpa.0000000000001996.
[35] Bick BL, Patel F, Easler JJ, et al. A comparative study between single-operator pancreatoscopy with intraductal lithotripsy and extracorporeal shock wave lithotripsy for the management of large main pancreatic duct stones. Surg Endosc 2022;36:3217–26. doi:10.1007/s00464-021-08631-7 .
[36] Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. N Engl J Med 2007;356:676–84. doi:10.1056/NEJMoa060610.
[37] Issa Y, Kempeneers MA, Bruno MJ, et al. Effect of early surgery vs endoscopy-first approach on pain in patients with chronic pancreatitis: the ESCAPE randomized clinical trial. JAMA 2020;323:237–47. doi:10.1001/jama.2019.20967.
[38] Talukdar R, Olesen SS, Unnisa M, et al. Extracorporeal shock-wave lithotripsy and endoscopy for the treatment of pain in chronic pancreatitis: a sham-controlled, randomized trial. Ann Intern Med 2024;177:749–58. doi:10.7326/m24-0210.
[39] Arvanitakis M, Ockenga J, Bezmarevic M, et al. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. Clin Nutr 2020;39:612–31. doi:10.1016/j.clnu.2020.01.004.
[40] Shimizu K, Ito T, Irisawa A, et al. Evidence-based clinical practice guidelines for chronic pancreatitis 2021. J Gastroenterol 2022;57:709–24. doi:10.1007/s00535-022-01911-6.