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Review

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Pancreatic extracorporeal shock wave lithotripsy: a key technology truly improves treatment model for pancreatic stones

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Abstract: Chronic pancreatitis (CP) is characterized by irreversible destruction of pancreatic parenchyma, inflammatory cell infiltration and progressive fibrosis of pancreatic tissue. Obstruction of pancreatic duct by pancreatic stone is the common pathological change in the course of CP with the incidence of over 50 % at the diagnosis of CP. These ductal stones would cause pancreatic parenchymal hypertension and local ischemia, which was eventually followed by recurrent episodes of painful pancreatitis or other manifestations of pancreatic exocrine and endocrine insufficiency. Removing pancreatic stones has been confirmed as the core to reduce pressure, improve drainage and lessen pain. Surgical therapy achieves satisfying pain relief with more complications, higher cost and less repeatability compared with endoscopic therapy. Endoscopic retrograde cholangiopancreatography, which used to be the standard endoscopic therapy for pancreatic stones, would fail if these stones are large or complex, while pancreatic extracorporeal shock wave lithotripsy (P-ESWL), which has been applied since 1987, could overcome this problem. Up to now, a large number of guidelines have recommended the P-ESWL as the first-line treatment strategy for radiopaque obstructive main pancreatic duct stones larger than 5 mm located in the head/body of the pancreas, and P-ESWL had completely changed the traditional treatment model for CP patients with pancreatic stones. In this article, we will focus on the technical progress, efficacy, safety and potential research areas of P-ESWL, we also give us suggestions for lithotripters improvement.

Keywords: chronic pancreatitis; pancreatic stones; pancreatic extracorporeal shock wave lithotripsy; treatment model

Introduction

Chronic pancreatitis (CP), characterized by irreversible destruction of pancreatic parenchyma, inflammatory cell infiltration and progressive fibrosis of pancreatic tissue, remains a challenging disease for both patients and clinicians now. Obstruction of pancreatic duct by pancreatic stone is the common pathological change in the course of CP with the incidence of over 50 % at the diagnosis of CP and 75.3 % within 15 years after the diagnosis of CP [1, 2]. These stones are radiopaque, radiolucent, or mixed type, and can be found in regions like the pancreatic head, body or tail, situating in the duct of pancreas, side branches or parenchyma of pancreas. It is worth noting that ductal stones would cause pancreatic parenchymal hypertension and local ischemia, which eventually followed by recurrent episodes of painful pancreatitis or other manifestations of pancreatic exocrine and endocrine insufficiency.

Fortunately, removing these pancreatic stones has been confirmed as the core to reduce pressure, improve drainage and lessen pain. Surgical therapy achieves satisfying pain relief rate in 68 %–89 % CP patients with pancreatic stones [3, 4]. Nevertheless, surgery carries more complications and higher cost. In addition, the anatomy has been significantly altered by severe adhesion in patients who have previously undergone pancreatic surgery, which contributes to the difficulty of a repeat operation for recurrence pancreatic stones [5]. On the contrary, endoscopic therapy is feasible to repeat with minimal invasive advantage. Endoscopic retrograde cholangiopancreatography (ERCP) and pancreatic sphincterotomy were used to be the standard endoscopic therapy for pancreatic stones.

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However, for radiopaque pancreatic stones >5 mm in size, balloon or baskets would fail because of these stones are dense, spiculated, and adherent to the ductal mucosa [6]. Pancreatic extracorporeal shock wave lithotripsy (P-ESWL), which has been applied since 1987, could overcome this problem [7]. Given the frequent changing of electrode and complex operation process, the P-ESWL had not been widely applied in the early application stage of P-ESWL. With the advent of modified lithotripters and development of technology since 20^{th} century, several large-scales centers in German, India, Japan and China, gradually optimized the P-ESWL procedure and formulated a standard treatment protocol. Up to now, P-ESWL has been verified as a safe and effective method to pulverize pancreatic stones, and numerous guidelines have recommended it as the first-line strategy for the clearance of radiopaque obstructive main pancreatic duct (MPD) stones larger than 5 mm located in the head/body of the pancreas [8–10].

P-ESWL had completely changed the traditional treatment model for CP patients with pancreatic stones. In this article, we will focus on the technical progress, efficacy, safety and potential research areas of P-ESWL, we also give us suggestions for lithotripters improvement.

Principle of P-ESWL

Lithotripters contain four components: shock wave generator, coupling device, focusing system and localization [11]. P-ESWL is based on the principle of shock wave energy. Firstly, pancreatic stones are localized by fluoroscopy or ultrasound, and then, a shock wave generator releases high-energy waves in an enclosed space. These high-energy waves are directed through focusing system onto the patient's abdominal wall, and the focal point targets stones. A coupling device is used to transmit shock waves to the skin surface and then through the body tissue. When these shock waves pass through substances of different acoustic impedance, compressive stress on the boundary surface is generated. This stress eventually overcomes the tensile strength of pancreatic stones and crumble the stones' anterior surface. Eventually, the shock waves cross through stones and are reflected from the stones' posterior surface, which contributes to further fragmentation [6, 11].

Global application of P-ESWL

An ideal multi-disciplinary treatment team for management of pancreatic stones should be composed by gastroenterologists, gastrointestinal surgeons, anesthetists, endoscopists, nurses and engineers of lithotripters. The requirement for this large and experienced team limits the application of P-ESWL procedure. Before 20th century, European countries including German, Belgium and Netherlands et al. were the main areas applying P-ESWL because of advanced machinery industry. Presently, centers in Asia–Pacific region reported large-volume patients and gradually became the places where P-ESWL was used most. The different type of abdominal pain may be the potential reason. In Asia–Pacific region, intermitted pain caused by stones obstruction is the main type of CP patients, and P-ESWL with ERCP could give complete clearance of MPD to achieve satisfactory pain relief. On the contrary, in Europe, pain in most CP patients is secondary to tissue and neural ischemia, neural entrapment, nociception, or visceral and central sensitization, which leads to continuous and persistent pain despite complete clearance of the MPD [12]. For these patients, pancreatic resection rather than P-ESWL may be a better choice to manage pain [13].

Technical progress of P-ESWL

In order to determine the development of P-ESWL, we found 27 articles including the description of lithotripters, anesthesia means, intensity energy and the number of shock waves per session in PubMed from 1987 to 2023 (Table 1). In the early application of P-ESWL, electrohydraulic lithotripter was the main machine for P-ESWL. Presently, electromagnetic or piezoelectric shock-wave-generating devices are commonly used because electrohydraulic lithotripter often cause large damage to tissues and need frequent equipment repair. Piezoelectric lithotripters are not as widely used as electromagnetic lithotripters now because they have lower energy levels and stone fragmentation efficiency. However, given the advantage of eliminating the need for electrode replacement compared with electromagnetic lithotripters, we speculate piezoelectric lithotripters will get wider application in the future.

Similarly, the patient's position during P-ESWL has also completely changed. Before 1986, patients were partly immersed in the water bath in supine position, while supine position or 30°-right supine position are the most used position now in order to more effective contact with shockwave head and simultaneously avoid the vertebrae and stones from overlapping in the image [30].

For the sake of large energy levels to adequately fragment pancreatic stones, the P-ESWL procedure itself is quite painful and anesthesia is necessary. Epidural anesthesia, general anesthesia or intravenous anesthesia are optional means. Epidural anesthesia and general anesthesia are commonly utilized in most centers, which are known to be invasive

Table 1: Study characteristics of pancreatic extracorporeal shock wave lithotripsy.

Author, year	Country	Sample size[a]	Lithotripters[b]	Intensity	Frequency (shock waves/min)	Number of shock waves per session	Treatment time per session, min	Anesthesia means[c]
Sauerbruch et al. 1987 [7]	Germany	1	Dornier HM3	18 kV	N/A	1,200	40	GA
Sauerbruch et al. 1989 [14]	Germany	8	Dornier HM3	18 kV	N/A	1,356	36	GA or IA
Kerzel et al. 1989 [15]	Germany	1	Wolf Piezolith 2300	Levels III–IV[d]	N/A	5,600	45	WOA
Delhaye et al. 1992 [16]	Belgium	123	Siemens Lithostar	10–19 kV	100	2,862	60	IA
Sauerbruch et al. 1992 [17]	Germany	24	Dornier HM3	18–24 kV	N/A	1,780	30–60	GA or IA
Van Der Hul et al. 1994 [18]	Netherland	17	Siemens Lithostar	16.2–19 kV	N/A	3,000–6,000	N/A	IA
Martin et al. 1995 [19]	USA	6	Dornier HM4	18–24 kV	N/A	1,200–2,400	N/A	IA
Wolf et al. 1995 [20]	USA	14	Dornier HM3	20 kV	N/A	2,000	N/A	IA
Schreiber et al. 1996 [21]	Austria	10	Dornier MPL 9000	19 kV	N/A	750	44	IA
Johanns et al. 1996 [22]	Germany	35	Dornier MPL 9000	14–22 kV	N/A	2,000	N/A	IA
Adamek et al. 1999 [23]	Germany	80	Wolf Piezolith 2300	Levels III–IV[d]	N/A	3,500	60	IA
Karasawa et al. 2002 [24]	Japan	24	Wolf Piezolith 2500	Levels III–IV[d]	N/A	4,200	N/A	WOA
Kozarek et al. 2002 [25]	USA	40	Dornier HM3	18–24 kV	N/A	1,800–2,400	N/A	GA or EA
Lawrence et al. 2010 [26]	USA	29	Storz Modulith SLX	7–8 kV	N/A	3,000–6,000	N/A	GA
Tandan et al. 2010 [27]	India	1,006	Dornier Delta Compact	15–16 kV	90	5,000	60–90	EA
Milovic et al. 2011 [28]	Germany	32	Storz Minilith SL 1	Adjusted to the individual[e]	N/A	6,800	N/A	WOA
Merrill et al. 2011 [29]	USA	30	Dornier HM3	Levels 3–9[d]	90–120	3,000–5,000	N/A	GA
			Storz Modulith SLX-F2	Levels 3–9[d]	90–120	3,000–5,000	N/A	GA
Li et al. 2014 [30]	China	634	Dornier Compact Delta II	10–16 kV	60–120	5,000	60–90	IA
Hu et al. 2016 [31]	China	214	Dornier Compact Delta II	16 kV	100	5,000	60–90	IA
Vaysse et al. 2016 [32]	France	146	Dornier Delta Compact	Adjusted to the individual[e]	100	1,200–6,000	N/A	IA
Tandan et al. 2019 [33]	India	5,124	Dornier Delta Compact	15–16 kV	90	5,000–6,000	N/A	EA
Korpela et al. 2016 [34]	Finland	83	Storz Modulith SLX	Levels 6[d]	60–90	3,000	N/A	N/A
			Storz Modulith SLX-F2	Levels 4[d]	60–90	3,000	N/A	N/A
Lapp et al. 2016 [35]	USA	37	Wolf Piezolith 3,000	18 kV	N/A	2,500	N/A	N/A
Hao et al. 2019 [36]	China	1,404	Dornier Compact Delta II	16 kV	120	5,000	60–90	IA
Liu et al. 2019 [37]	China	106	Dornier Compact Delta II	16 kV	100	5,000	60–90	IA

Table 1: (continued)

Author, year	Country	Sample size[a]	Lithotripters[b]	Intensity	Frequency (shock waves/min)	Number of shock waves per session	Treatment time per session, min	Anesthesia means[c]
Hyun et al. 2021 [38]	USA	97	Storz Modulith SLX-F2	Levels 6–7[d]	N/A	3,000–5,500	N/A	GA
Ito et al. 2023 [39]	Japan	208	Storz Modulith SLX-F2 Siemens Lithostar Siemens Lithoskop	Adjusted to the individual	45–60	2,000	N/A	LA

[a]Some studies have sample size overlaps: the sample size of reference [7] is included in reference [15]; the sample size of reference [28] is included in reference [33]; the sample size of reference [31] is included in reference [30], and they are all included in reference [36]. [b]The type of lithotripter is represented by company name and machine model. [c]GA, general anesthesia; IA, intravenous anesthesia; EA, epidural anesthesia; LA, local anesthesia; WOA, without anesthesia. [d]Only energy level settings are available in studies, and specific energy parameters are unknown. [e]"adjusted to the individual" means energy level or number of shock waves are tailored to the individual pain tolerance of the patient.

procedures due to the involvement of tracheal intubation or epidural puncturing, and both of these have long induction and/or recovery periods [40]. Target-controlled infusion of remifentanil with flurbiprofen axetil is proven to provide satisfactory analgesia and sedation for P-ESWL, while the involuntary movement of patients is inevitable, which would lead to stone location bias and adjacent tissue damage [41].

High intensity energy and more shock wave numbers per session have become the dominant models in the world with the development of lithotripters. This is reasonable because pancreatic stones are so hard to pulverize completely by low intensity energy and fewer shock wave numbers. Five thousands to six thousands shocks per session at a rate of 90–2120/min and energy level of 16 kV is the most used model in P-ESWL now.

We have formulated a standard P-ESWL protocol in our center from 2011 and more than 15,000 procedures have been performed so far. CP patients admitted to our center would firstly receive a contrast-enhanced computed tomography with/without contrast-enhanced magnetic resonance imaging to confirm the presence and size of pancreatic stones. Radiopaque obstructive MPD larger than 5 mm located in the head/body of the pancreas is the indications for P-ESWL, and MPD stones that are radiolucent or smaller than 5 mm should receive ERCP as the first-line treatment strategy [8]. In our center, an electromagnetic lithotripter (Compact Delta II; Dornier Med Tech., Wessling, Germany) with bi-dimensional fluoroscopic targeting facility is used for P-ESWL, and intravenous remifentanil combined with flurbiprofen is administered for analgesia during the procedure. Patients are placed in the supine position or tilted to their right side at an angle of 30° (Figure 1). A maximum of 5,000 shock waves per session are delivered at a frequency of 60–120 shocks per minute and an intensity of 6 (16 kV) on a scale of 1–6 is used during the procedure. The duration of each session is 60–90 min. Fluoroscopy monitors the fragmentation of the stones, and repeat P-ESWL sessions could performed on successive days until the stones have been fragmented to 3 mm or less in size. As far as patients with complications after P-ESWL, the next P-ESWL session is recommended when the patient has recovered from complications. ERCP is routinely perform after the last P-ESWL session to remove stone fragments and complete the visualization of pancreatic duct system. Singal or multiple pancreatic stents (5–10 Fr) are placed in patients with dominant MPD stricture, MPD rupture, or pseudocyst that necessitated stent placement for drainage. Once the MPD is free of any pathology, these stents are removed at a subsequent follow-up between 3 and 12 months [5, 30, 31, 42, 43].

Technical and clinical success of P-ESWL

The rate of MPD stones clearance and pain relief in different studies had great difference depending on the different lithotripters and research years (Table 2) [6, 31, 44, 45]. Retrospective single-center research in India analyzed 5,124 patients subjected to P-ESWL, among these patients, 4,386 (85.5 %) patients required 3 or fewer sessions for fragmentation and 3,722 (72.6 %) patients achieved complete stone clearance. Four thousand two hundred and 80 patients were followed up for 6 months and 3,529 (82.6 %) had pain free [44]. In Japan, the complete stone clearance rate was 74.3 %, and 90.9 % patients got symptom relief [46]. A meta-analysis including 22 studies indicated that the complete

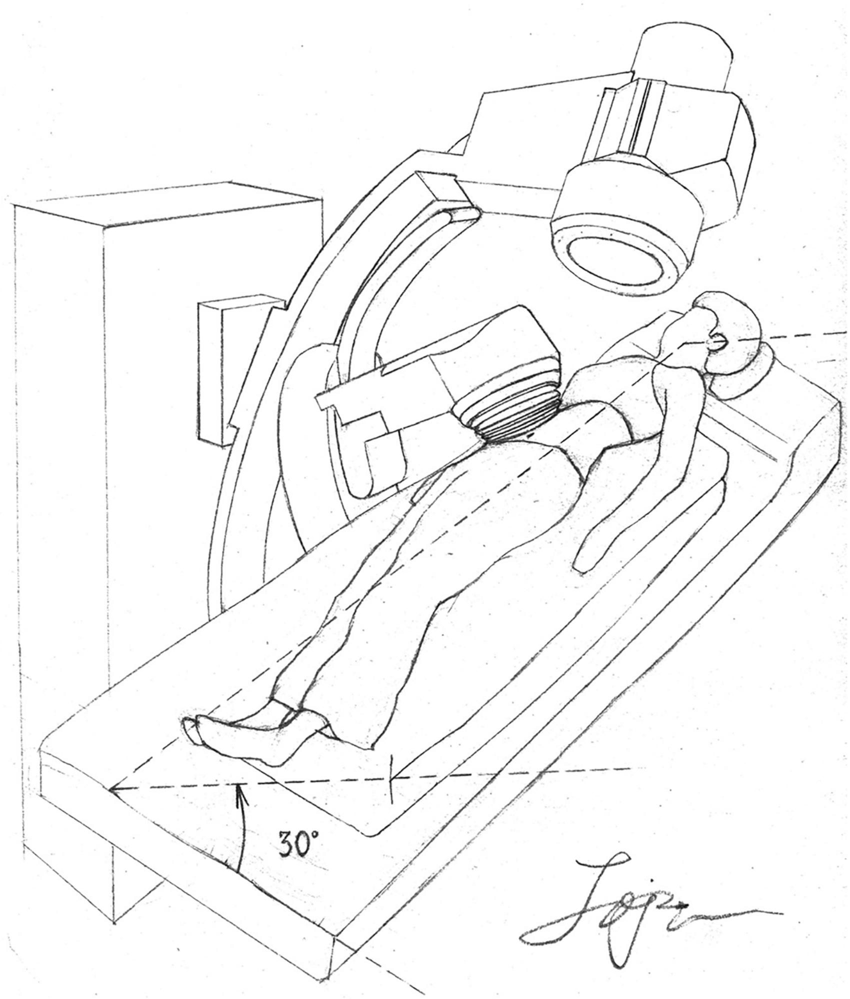

Figure 1: Position of patient for pancreatic extracorporeal shock wave lithotripsy.

ductal clearance was 69.8 % and the pooled proportion of complete absence of pain during follow-up was 64.2 % [47].

In our experience, 84.6 % patients received 3 sessions or fewer of P-ESWL for adequate fragmentation, and only 2.3 % patients require 6 sessions or more. Complete clearance of MPD stones were achieved in 155 (72.4 %) patients. Follow-up after 18.5 ± 3.3 months showed that the rates of complete and partial pain relief were 71.3 and 24.0 %, respectively. Both scores for the quality of life and mental health from the Medical Outcomes Study 36-Item Short-Form General Health Survey questionnaire were improved after P-ESWL [31].

Adverse events of P-ESWL

The mechanisms of adverse events may be as follows. Firstly, the energy of shock wave will be released before reaching the target stones. Secondly, due to the position of stones always changing with the respiratory motion, it is difficult for us to localize the stones in the focal point accurately. Thirdly, if intravenous analgesia is chosen for analgesia and sedation, the involuntary movement of patients is unavoidable. These three reasons would all lead to the part of energy releasing along the shock wave conducting pathway or around the stones rather than hitting the stones precisely. Because the anatomic location of organs along the shock wave conducting pathway differs greatly, adverse events after P-ESWL are varied and difficult to predict.

The established definition and classification for the adverse events after P-ESWL were lacking. In 2014, Li et al. firstly proposed a criterion for post-ESWL adverse events based on hospitalization days and the interventions required to treat adverse events [30]. According to the severity, adverse events can be classified as either complications or transient adverse events (TAEs).

TAEs include skin erythema, mild tenderness of the region in contact with the shockwave head, asymptomatic hyperamylasemia, hematuria, and acute gastrointestinal mucosal injury (manifested as hematemesis and melena), which are transient and reversible requiring no medical

Table 2: MPD clearance and pain relief after performing pancreatic extracorporeal shock wave lithotripsy.

Source	Sample size[a]	Type	MPD clearance	Follow-up (from P-ESWL procedure)	Pain relief
Sauerbruch et al. 1992 [17]	24	Prospective	Completely clearance: 42 %; Partially clearance: 29 %	24 months	Completely and partially relief: 83 %
Delhaye et al. 1992 [16]	123	Prospective	Completely clearance: 59 %	14 months	Completely relief: 38 %
Van Der Hul et al. 1994 [18]	17	N/A	Completely clearance: 41 %	30 months	Completely and partially relief: 42 %
Martin et al. 1995 [19]	6	Retrospective	Completely clearance: 83 %; Partially clearance: 17 %	19 months	Completely relief: 100 %
Wolf et al. 1995 [20]	12	Retrospective	Completely clearance: 58 %; Partially clearance: 33 %	19–22 months	Completely relief: 33 %; Partially relief: 33 %
Schreiber et al. 1996 [21]	10	N/A	Completely and partially clearance: 70 %	12 months	Completely and partially relief: 70 %
Johanns et al. 1996 [22]	35	N/A	Completely clearance: 46 %; Partially clearance: 54 %	23 months	Completely relief: 34 %; Partially relief: 49 %
Costamagna et al. 1997 [48]	35	N/A	Completely clearance: 74 %	27 months	N/A
Adamek et al. 1999 [23]	80	N/A	Completely and partially clearance: 53 %	40 months	Completely and partially relief: 76 %
Farnbacher et al. 2002 [49]	114	Retrospective	Completely clearance: 34 %; Partially clearance: 48 %	29 months	Completely relief: 48 %
Karasawa et al. 2002 [24]	24	N/A	N/A	12 months	Completely and partially relief: 46 %
Tandan et al. 2010 [27]	1,006	Prospective	Completely clearance: 76 %; Partially clearance: 17 %	6 months	Completely and partially relief: 84 %
Lawrence et al. 2010 [26]	29	N/A	Completely and partially clearance: 59 %	35 months	Completely and partially relief: 60 %
Parsi et al. 2010 [50]	10	Prospective	Completely clearance: 70 %; Partially clearance: 30 %	20 months	Completely and partially relief: 70 %
Milovic et al. 2011 [28]	32	Prospective	Completely clearance: 41 %	N/A	Completely and partially relief: 75 %
Seven et al. 2012 [51]	120	Retrospective	N/A	52 months	Completely relief: 50 %; Partially relief: 35 %
Suzuki et al. 2013 [46]	479	Retrospective	Completely clearance: 74 %	31 months	Completely relief: 76 %
Li et al. 2016 [42]	59	Prospective	Completely clearance: 64 %; Partially clearance: 21 %	12 months	Completely relief: 64 %; Partially relief: 26 %
Lapp et al. 2016 [35]	37	Retrospective	Completely clearance: 80 %	3 months	Completely and partially relief: 95 %
Korpela et al. 2016 [34]	83	Retrospective	Completely and partially clearance: 64 %	53 months	Completely and partially relief: 93 %
Vaysse et al. 2016 [32]	146	Retrospective	Completely clearance: 56 %	6 months	Completely and partially relief: 76.0 %
Hu et al. 2016 [31]	214	Prospective	Completely clearance: 72 %; Partially clearance: 15 %	19 months	Completely relief: 71 %; Partially relief: 24 %
Wang et al. 2017 [43]	72	Prospective	Completely clearance: 86 %	36 months	Completely relief: 78 %
Haraldsson et al. 2018 [52]	81	Retrospective	N/A	N/A	Completely relief: 40 %
Wang et al. 2018 [5]	50	Prospective	Completely clearance: 77 %	31 months	Completely relief: 60 %
Tandan et al. 2019 [33]	5,024	Retrospective	Completely clearance: 73 %; Partially clearance: 17 %	6 months	Completely relief: 83 %; Partially relief: 12 %
Hao et al. 2019 [36]	72	Prospective	Completely clearance: 74 %	48 months	Completely relief: 79 %
Yamamoto et al. 2022 [45]	165	Retrospective	Completely and partially clearance: 79 %	Short-term	Completely and partially relief: 94 %
Bick et al. 2022 [53]	240	Retrospective	Completely clearance: 87 %	N/A	Completely and partially relief: 83 %

[a]Some studies have sample size overlaps: the sample size of reference [28] is included in reference [33]. MPD, main pancreatic duct; P-ESWL, pancreatic extracorporeal shock wave lithotripsy.

intervention and prolonged hospitalization. According to the experience from America, the rate of TAEs after P-ESWL was approximately 15 %, and most cases were skin erythema [25]. In India, skin erythema and pain at the site of delivery of shocks were common reports, with incidences of 19 and 13.5 %, respectively [33]. In China, the rate of TAEs was approximately 21.2 %, and asymptomatic hyperamylasemia was the most common TAE with a rate of 15.5 %. The rate of hematuria was approximately 4.2 %. The prevalence of acute gastrointestinal mucosal injury was 2.7 % after P-ESWL [30].

On the contrary, complications refer to adverse events needing specific medical intervention and prolonged hospitalization, which can be classified into five groups: post-ESWL pancreatitis, bleeding, infection, steinstrasse and perforation. Each group of complications can also be classified as mild, moderate or severe on the basis of the length of hospitalization days and subsequent treatment (Table 3) [30]. Post-ESWL pancreatitis has been confirmed to be the most common complication after P-ESWL in Japan and America with the incidence of 4.4 %, 2.5 %, respectively [25, 54]. According to the experience in India, post-ESWL pancreatitis can be seen in 3.6 % of patients, and 0.5 % among them required hospitalization for more than 3 days [33]. In China, the overall complication rate was approximately 6.73 %, with incidences of post-ESWL pancreatitis, infection, steinstrasse, bleeding and perforation of 4.35 %, 1.4 %, 0.4 %, 0.3 % and 0.3 %, respectively.

In addition, some rare complications have been reported but not included in this classification of adverse events, such as splenic rupture, hepatic subcapsular hematoma, colonic hematoma, acute renal failure, hemorrhagic pseudoaneurysm, pancreaticobiliary fistula, intussusception, lung contusion and hepatic abscess et al. [55–64].

A large number of studies have proven the safety P-ESWL, and even among special populations, such as pediatric patients, geriatric patients, patients with a history of pancreatic surgery or patients with pancreatic pseudocyst, P-ESWL also has a low risk of complications [5, 36, 42, 43].

Table 3: Definitions of major complications of pancreatic extracorporeal shock wave lithotripsy [30].

Complication[a]	Mild	Moderate	Severe
Post-ESWL pancreatitis	Clinical pancreatitis, amylase at least three times the normal level at >24 h after procedures, require admission or extension of planned admission from 2 to 3 days	Requires hospitalization of 4–10 days	Hospitalization for 10 days, pseudocyst or intervention (percutaneous drainage or surgery)
Bleeding[b]	Clinical evidence of bleeding, hemoglobin drop <3 g, no transfusion	Transfusion of ≤a units, no angiographic intervention, or surgery	Transfusion of ≥a units or intervention (angiographic or surgery)
Infection	>38 °C for 24–48 h	Require >3 days of hospital treatment	Abscess, septic shock, or intervention (percutaneous drainage or surgery)
Steinstrasse	Severe abdomen pain without other post-ESWL complications	Combined with other complications, or requires >3 days of hospital treatment	Combined with other complications; hospitalization >10 days, or surgery
Perforation	Possible, or very slight leak of fluid, treatable with fluids and suction for ≤3 days	Any definite perforation treated medically for 4–10 days	Medical treatment for >10 days or intervention (percutaneous or surgical)

ESWL, extracorporeal shock wave lithotripsy. [a]Splenic rupture, pancreaticobiliary fistula, and other rare complications are not included in this classification of complications. [b]Acute gastrointestinal mucosal injury was not included; it was classified as a transient adverse event.

P-ESWL vs. pancreatoscopy-guided lithotripsy

Pancreatoscopy-guided lithotripsy is recommended when P-ESWL is not available or pancreatic stones are not fragmented after adequately performed P-ESWL [8]. Pancreatoscopy-guided lithotripsy is an emerging and booming technique with numerous studies for its efficacy and safety. However, there is little research about comparing P-ESWL with pancreatoscopy-guided lithotripsy. A retrospective cohort study performed in USA included 240 patients treated with P-ESWL and 18 treated with pancreatoscopy-guided lithotripsy. P-ESWL and pancreatoscopy-guided lithotripsy groups had similar technical success rates (86.7 % vs. 88.9 %, p=1.000) and adverse event rates (6.3 % vs. 5.6 %, p=1.000). Compared with P-ESWL, pancreatoscopy-guided lithotripsy group required fewer total procedures (1.6 ± 0.6 vs. 3.1 ± 1.5, p<0.001) and shorter aggregate procedure time (101.6 ± 68.2 vs. 191.8 ± 111.6 min, p=0.001).

Pancreatoscopy-guided lithotripsy has some potential advantages. First, pancreatoscopy-guided lithotripsy allows visualize pancreatic stones directly and target stones accurately, which cannot be accomplished easily by P-ESWL because stones may move in and out of focal point during the respiratory cycle. Second, radiolucent stones can be directly seen with pancreatoscopy-guided lithotripsy. Last but not least, pancreatoscopy-guided lithotripsy is a step in ERCP, while P-ESWL requires subsequent ERCP procedures to clear stones fragment [53]. Across downstream MPD strictures by pancreatoscope difficultly is the main limitation of pancreatoscopy-guided lithotripsy, which is the most common reason for the failure of pancreatoscopy-guided lithotripsy [65]. Nevertheless, P-ESWL can target stones throughout the pancreas. Overall, P-ESWL and pancreatoscopy-guided lithotripsy have their own advantages and disadvantages, and physicians should choose a reasonable lithotripsy method according to the specific conditions of the stone and the conditions of the medical center.

Potential research areas about P-ESWL

According to our previous study, there were no procedure-related factors independently increased the risk of adverse events after P-ESWL. However, in that study, the data for risk factor analyses were limited and the maximum number of shock waves in a single P-ESWL session was 5,000 shocks, which contributed the biased results [30]. The existing literature on urinary ESWL has demonstrated shock wave frequency and the number of shock waves were important factors for the adverse events after ESWL [66, 67]. Identifying procedure-related factors can improve treatment protocols and affect the outcome of P-ESWL. A further study would pay more attention to the procedure-related risk factors about P-ESWL.

It has previously been observed that a shock wave rate varies from 60 to –120 shocks per minute in different studies, and there is a debate on which one is the most efficacy and safety frequency. Shock waves at a lower frequency may reduce the incidence of adverse events after P-ESWL, but likely to increase exposure times. On the contrary, shock waves at a higher frequency have a tendency to reflect from the stones and interfere with the efficacy of oncoming shockwaves [11]. A meta-analysis about urinary ESWL reported that patients treated at a rate of 60 shocks per minute have a significantly greater likelihood of a successful treatment outcome than 120 shocks per minute [67]. Tandan et al. suggested that a shock wave rate of 90 shocks per minute is ideal for fragmenting pancreatic stones despite lacking researches [6]. Further data collection is required to determine exactly which frequency is optimal for P-ESWL.

The standard protocol for fragmenting pancreatic stones is unchanged and not adjusted according to the size and density of stones in different patients in most centers. Inappropriate treatment procedure may lead to lower success rate, higher adverse events rate or medical cost. Non-contrast computed tomography (NCCT) has been proved as the optimal predictor for P-ESWL efficacy, and mean stone density >1,000.45 HU has a close relationship with reduced stone clearance rate, while mean stone density <375.4 HU on NCCT has a better fragmentation [68, 36]. Additionally, NCCT may help clinician identify those patients who should avoid P-ESWL because of high stone density [6]. Treatment procedure should be adjusted on basis of NCCT of pancreatic stones, and personalized treatment strategy may become an important research area in the future.

Another potentially fruitful avenue for future research is how to prevent adverse events after P-ESWL, and studies on this field remain few. Up to date, only one prospective randomized controlled study found preoperative use of nonsteroidal anti-inflammatory drugs (NSAIDs) which has been confirmed the role of preventing post-ERCP pancreatitis (PEP) could also reduce post-ESWL pancreatitis from 12 % to 9 % [69]. However, previous studies have suggested various mechanisms leading to PEP, and post-ESWL pancreatitis has the potentially similar pathogenesis as PEP [70]. Given to this, prevention measures for PEP, such as pancreatic stents, intravenous fluids, or combinations of these, may also have the function for prophylaxis of post-ESWL pancreatitis [71–74].

Effect of pancreatic stents during P-ESWL procedure has not been clarified. The potential advantages of keeping pancreatic stent during P-ESWL are that: (1) increasing the accuracy of targeting stones in MPD; (2) decreasing the rate of post-ESWL pancreatitis as it does in ERCP [73]. However, keeping the stent during P-ESWL also has significant drawbacks. Intraductal stent may impede spontaneous clearance of stone after P-ESWL as the size of fragmented stone may still exceed the inner diameter of the largest plastic stent (10 Fr) and stent retained for over 3 months is at high risk of occlusion. Kondo et al. demonstrated pancreatic stents prior P-ESWL helped to decrease the cumulative number of shock waves required for stones fragmentation and shortened the duration of therapy while did not reduce post-ESWL pancreatitis [75]. Nevertheless, the necessity and cost efficiency to perform a pre-ESWL ERCP in all patients to confirm the presence of MPD stones and evaluate the feasibility of stone extraction are still unknow [76]. Moreover, no previous studies have explored the effect of pancreatic stent on spontaneous clearance of stone.

Previous studies have indicated using diuretics before ESWL is a useful, inexpensive and safe method to increase the effect of ESWL on ureteric stones [77, 78]. Therefore, secretin may also relate to superior stone fragmentation and clearance compared with standard P-ESWL. The first study about the role of secretin during P-ESWL had been presented by Choi et al. and the results proved that intravenous secretin appears to aid clearance of MPD stones in CP patients [79]. Researchers discussed the potential reasons. First, secretin created a liquid-filled space surrounding the stones or within stones for better stones disintegration by focused shock waves [80, 81]. Second, secretin can also facilitate flushing out stone fragments during P-ESWL [79]. However, the studies about secretin were limited and further prospective randomized studies are needed to examine the role of secretin during P-ESWL.

Epidural anesthesia, general anesthesia or intravenous anesthesia have been well accepted in most centers as satisfactory strategy for P-ESWL. However, each has its advantages and drawbacks, and few studies have been performed to investigate the most suitable anesthetic technique for P-ESWL.

Although P-ESWL has been proved as a less invasive and higher efficacy procedure to treat pancreatic stones in large volume centers, stone recurrence occurs in 22 %–38 % of patients who had complete MPD clearance over long-term follow-up [45, 82]. Unfortunately, only Yokoyama et al. have examined the risk factors for pancreatic stones recurrence, and they found the visceral-to-subcutaneous adipose tissue area ratio was related to retreatment ratio after P-ESWL [83]. More researches need to be undertaken on the topic of pancreatic stones recurrence.

Advices for lithotripters improvement

The introduction from water tub-style to dry-head was an important advance in the evolution of lithotripsy, while the efficacy seemed decreases in the new generation lithotripters. Several studies have suggested the bubbles in the coupling medium would affect the transmission of the shock wave into the patient. Coverage by air pockets of only 2 % could dramatically reduce stone breakage efficiency by 20 %–40 % [84]. In 2014, Tailly et al. installed standard incorporation of an optically controlled coupling system in lithotripters to decrease the energy loss caused by air bubbles and the total applied energy was exactly reduced compared with a “blind” coupling mode [85].

Localizing the pancreatic stones in the focal point accurately is a technological difficulty due to the position of pancreas always changes with the respiratory motion. In urinary ESWL, an ultrasound-based, real-time stone tracking system has been used to decrease stone misidentification. The tracking system would be activated when it identifies stones, and then the shock wave generator track will send out shock waves to the stone. Otherwise, when stones cannot be identified because stones leave out of the 2-dimensional ultrasound scan plane, the tracking system would fail, and no shock wave could be sent out until stones could be monitored next time [86, 87].

These two technological improvements have been applied to urinary stones, but there are no reports for pancreatic stones.

Summary

A standard protocol of P-ESWL has been formulated, and it is a safe and effective procedure for the management of pancreatic stone. However, there are also many improvements should be made for higher efficiency, lower rates of adverse events and more cost-effectiveness.

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