Digital single-operator pancreatoscopy for the treatment of symptomatic pancreatic duct stones: a prospective multicenter cohort trial

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ABSTRACT

Background Digital single-operator pancreatoscopy (DSOP)-guided lithotripsy is a novel treatment modality for pancreatic endotherapy, with demonstrated technical success in retrospective series of between 88 % and 100 %. The aim of this prospective multicenter trial was to systematically evaluate DSOP in patients with chronic pancreatitis and symptomatic pancreatic duct stones.

Methods Patients with symptomatic chronic pancreatitis and three or fewer stones ≥ 5mm in the main pancreatic duct (MPD) of the pancreatic head or body were included. The primary end point was complete stone clearance (CSC) in three or fewer treatment sessions with DSOP. Current guidelines recommend extracorporeal shock wave lithotripsy (ESWL) for MPD stones > 5 mm. A performance goal was developed to show that the CSC rate of MPD stones using DSOP was above what has been previously reported for ESWL. Secondary end points were pain relief measured with the Izbicki pain score (IPS), number of interventions, and serious adverse events (SAEs).

Results 40 chronic pancreatitis patients were included. CSC was achieved in 90 % of patients (36/40) on intention-to-treat analysis, after a mean (SD) of 1.36 (0.64) interventions (53 procedures in total). The mean (SD) baseline IPS

decreased from 55.3 (46.2) to 10.9 (18.3). Overall pain relief was achieved in 82.4 % (28/34) after 6 months of follow-up, with complete pain relief in 61.8 % (21/34) and partial pain relief in 20.6 % (7/34). SAEs occurred in 12.5 % of patients (5/40), with all treated conservatively.

Conclusion DSOP-guided endotherapy is effective and safe for the treatment of symptomatic MPD stones in highly selected patients with chronic pancreatitis. It significantly reduces pain and could be considered as an alternative to standard ERCP techniques for MPD stone treatment in these patients.

Introduction

Pain is the dominating symptom of chronic pancreatitis, causing a reduction of quality of life, more unemployment, and major healthcare costs [1]. The pathophysiology of pain in chronic pancreatitis is multifactorial, but is mainly generated by localized pathology, such as focal pancreatic duct (PD) obstruction and/or a localized inflammatory mass [2–5]. Analgesics are the cornerstone of pancreatic pain management [6]. Chronic pancreatitis with obstruction of the PD is associated with intraductal calculi in 50 % of patients, with 18 % being caused by PD stones and 32 % by a combination of PD stricture and PD stone [7].

When analgesic therapy fails, invasive treatment with endoscopic PD clearance (with or without extracorporeal shock wave lithotripsy [ESWL] or PD dilation and/or stenting) are the next treatment steps [3, 8]. Guidelines recommend endoscopic therapy and/or ESWL as the first-line therapy for painful uncomplicated chronic pancreatitis with an obstructed main pancreatic duct (MPD) in the head/body of the pancreas [1, 8]. The rationale for invasive treatments is that reducing the ductal pressure by restoring the flow of pancreatic juice will result in pain relief [8].

Major limitations of ESWL include limited availability, lack of reimbursement in different countries, the need for (general or epidural) anesthesia, variable efficacy (depending on the experience of the operator and/or location and size of the PD stones), and the frequent need for additional endoscopic retrograde cholangiopancreatography (ERCP) if there is a dominant PD stricture [1, 8, 9].

Digital single-operator pancreatoscopy (DSOP)-guided lithotripsy (▶ **Fig. 1**) seems to be an attractive alternative to ESWL in patients with chronic pancreatitis with PD dilatation [10, 11]. Additionally, DSOP can be combined with a subsequent intervention, such as PD stricture dilation and/or PD stenting in one session. A recent meta-analysis on DSOP for difficult PD stones reported a technical success rate of 91 % and an adverse event (AE) rate of 14 % [10].

Although DSOP has shown promising results in chronic pancreatitis, studies to date have been limited by their retrospective design, relatively small patient populations, short follow-up, lack of useful clinical end points, variety of patient selection/treatment regimens, and often their single-center design [4, 5]. In this study, we report the results of a prospective multicenter study that aims to address these limitations. Patients were followed up for at least 6 months after the last DSOP. Here, we present the results for technical success, pain relief, and AEs.

Methods

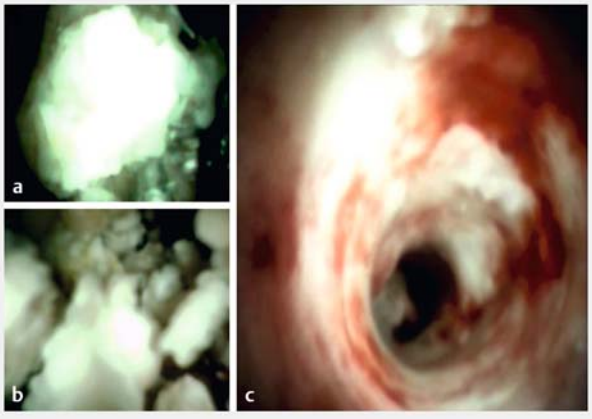
Study design

This prospective clinical trial was conducted in tertiary referral centers in Germany, Switzerland, the Netherlands, and Italy. The study protocol was designed in accordance with the Helsinki declaration, and approved by the Medical Ethics Committee of each participating center. The study objective was to determine the effectiveness and safety of DSOP (SpyGlass DS; Boston Scientific Corp., Natick, Massachusetts, USA) in the treatment of pain resulting from obstructive chronic pancreatitis with a dilated PD and MPD stones.

Patients

Adult patients with severe pain due to chronic pancreatitis with a dilated PD and MPD stones with progressive pain were eligible for enrollment. Patients were screened for eligibility including stone size and MPD size with magnetic resonance imaging (MRI), and/or computed tomography (CT) or endoscopic ultrasonography (EUS). A multidisciplinary pancreatic expert board assessed the diagnosis of chronic pancreatitis according to European guidelines, along with the indication for endoscopic treatment [1].

Patients aged over 18 years with chronic pancreatitis were invited by their treating physician to participate in the study after



▶ **Fig. 1** Example images of digital single operator pancreatoscopy-guided lithotripsy showing: **a** a lumen-occluding stone with the electrohydraulic lithotripsy probe on the stone; **b** fragmentation of the stone; **c** complete duct clearance after removal of the stone fragments.

they had been screened against the inclusion and exclusion criteria. The inclusion criteria were recurrent pain episodes for at least 3 months, three or fewer radiopaque stones with a diameter of ≥ 5 mm restricted to the pancreatic head, genu, or corpus with obstruction of the MPD, and written informed consent.

The exclusion criteria included: a contraindication to ERCP (poor health status [American Society of Anesthesiologists (ASA) classification system ≥ 4]); pregnancy; and coagulopathy (international normalized ratio [INR] ≥ 2, platelet count < 70 / nL, or intake of antiplatelet agents or anticoagulants other than aspirin in the preceding 7 days). Further exclusion criteria were: a history of chronic pancreatitis of more than 3–4 years; daily use of opioids, except tramadol, for more than 6 months in the last 2 years; altered gastrointestinal anatomy with no endoscopic approach to the papilla; prior ESWL therapy; and other severe interfering conditions of the biliopancreatic tract, such as autoimmune pancreatitis, pancreatic cancer, an episode of biliary obstruction in the previous 2 months, symptomatic walled-off necrosis (WON), or more than one MPD stricture.

All interventions were discussed by the multidisciplinary pancreatic expert board in the predefined chronic pancreatitis expert centers before and after the procedure. Once the local expert board had confirmed eligibility, patients were treated with DSOP. Where DSOP failed, alternative strategies (i. e. ESWL/ERCP, surgery, or conservative management) were discussed by the same team.

Study data were anonymously registered at each study site in a secure online database using a study code. Only the principal investigator had access to the study codes. Baseline characteristics and outcomes were collected and stored securely by a local study nurse during hospital admission, using a standardized case report form (CRF) as a hard copy. In addition, the data were anonymously (using a patient study code) entered onto a secure web-based database.

Outcomes

The primary end point was technical success, defined as complete stone clearance (CSC) of the MPD in three or fewer treatment sessions on ERCP and DSOP images. Secondary end points included: the Izbicki pain score (IPS) before and after treatment at 3 and 6 months after the last intervention; number of treatment sessions; PD diameter before treatment and at 6 months after the final intervention; visualization of the stone with DSOP; successful drainage after complete/incomplete fragmentation; successful PD stent placement if needed; and AEs at 24 hours, 30 days, 3 months, and 6 months after intervention.

Definitions

Clinical outcome was measured using the IPS [12]. Complete relief was defined as an IPS ≤ 10; partial relief was defined as an IPS > 10 but showing a decrease of > 50 % compared with the baseline score. AEs were defined according the European Society of Gastrointestinal Endoscopy (ESGE) and United European Gastroenterology (UEG) guidelines [8, 13, 14]. Chronic pancreatitis is defined as a pancreatic disorder in which recurrent inflammatory episodes result in replacement of the pancreatic parenchyma by fibrous connective tissue [1]. Post-ERCP-pancreatitis (PEP) was defined as new or worsened abdominal pain combined with > 3 times the normal value of amylase or lipase at more than 24 hours after ERCP and requirement for admission or prolongation of a scheduled admission [13]. PD diameter was assessed at the widest point of the upstream duct dilatation.

Endoscopic procedure

DSOP and alternative procedures were performed by experienced endoscopists and surgeons. An experienced endoscopist was defined as having performed at least 200 ERCPs and over 20 DSOP procedures per year, for at least the preceding 2 years before initiation of the study.

Sedation or general anesthesia were provided according to the individual protocol of each participating center. Before the intervention, laboratory parameters such as hemoglobin, white blood cells (WBC), C-reactive protein (CRP), and lipase were assessed.

Pancreatic sphincterotomy and balloon dilation of a stricture downstream were performed prior to DSOP. The pancreatoscope was advanced either over a guidewire or freehand. Lithotripsy was performed using electrohydraulic lithotripsy (EHL) or laser lithotripsy. Intermittent MPD irrigation with saline was used for stone visualization, with the irrigation volume being as small as possible to minimize the risk of PEP. Procedures were ended at the discretion of the endoscopist. Reasons for procedure abortion included a nonsignificant change in stone size after 1000 shots (counted by the lithotripter). After completion of lithotripsy, stone fragments were extracted using balloon or basket catheters, followed by pancreatic plastic stent placement for 3 months to prevent PEP and provide MPD decompression. After 3 months, a new stent was only placed if there was an ongoing stricture. Prophylactic rectal nonsteroidal anti-inflammatory drugs (NSAIDs) were administered prior to the treatment.

All patients were routinely admitted post-DSOP for 24 hours and screened for serious AEs (SAEs), especially PEP [13]. A blood sample for hemoglobin, WBC, CRP, and lipase was taken 1 day after the intervention or earlier if needed. Pain was documented immediately after the DSOP, at 24 hours, and before the patient was discharged. In addition, 30 days after the procedure, patients were interviewed by telephone to evaluate any symptoms or delayed complications.

Follow-up

Patients with failed duct clearance in the index session were rescheduled for a subsequent DSOP intervention within 3 months. The maximum number of DSOP-based interventions was limited to three. In patients with successful stone clearance, an magnetic resonance cholangiopancreatography (MRCP) or CT, and/or EUS of the pancreas was performed at 6 months after treatment. In addition, patients were interviewed regarding SAEs and to assess their IPS at 3 months and 6 months after the final DSOP.

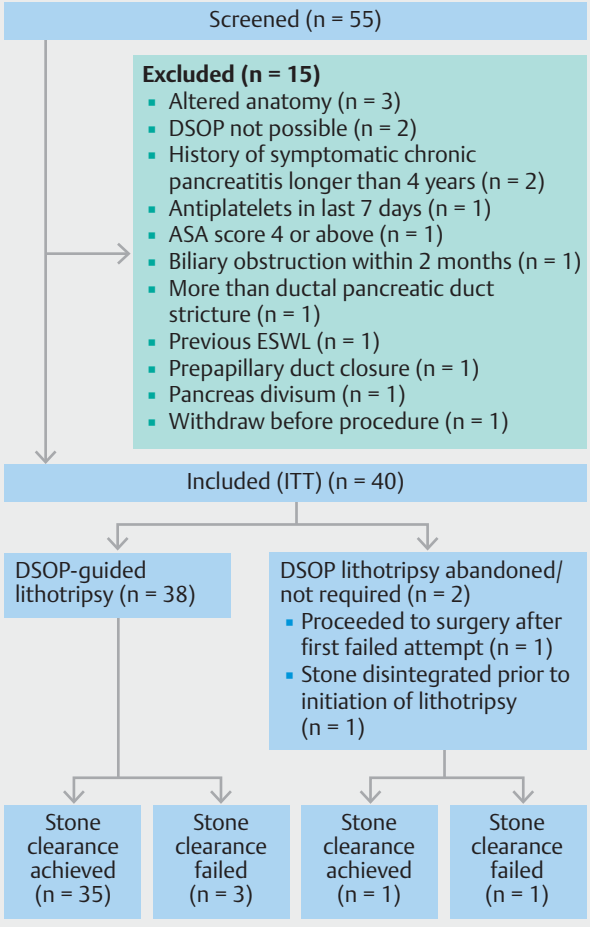
Statistical methods

Sample size calculation

A performance goal was developed to show that the rate of complete clearance of MPD stones using DSOP was above that reported in the literature for ESWL. This performance goal for ESWL was taken from a published meta-analysis and was set at 74 % [15]. The assumed rate of success for DSOP was taken from the literature and set at 90 % [4, 5, 16]. For an exact one-sided test with a power of 80 %, it was calculated that 43 patients would be required to enroll to show that the success rate of DSOP was above 74 %.

Statistical analysis

Continuous measures were analyzed using mean and SD. Binary variables were reported as rates, with the denominator using the available data reported from each site. The primary end point was evaluated using a one-sided exact test, while all other end points were evaluated using a two-sided test. The change



▶ **Fig. 2** Flowchart of inclusion and exclusions from the study. ESWL, extracorporeal shock wave lithotripsy; ASA, American Society of Anesthesiologists; ITT, intention to treat; DSOP, digital single operator pancreatoscopy.

▶ **Table 1** Demographics and baseline characteristics of the 40 patients who underwent digital single-operator pancreatoscopy for chronic pancreatitis with three or more main pancreatic duct stones.

Age, years	
▪ Mean (SD)	56.7 ± 15.5
▪ Median (range) [IQR]	58.6 (23.6 to 81.5) [42.8 to 69.1]
Sex, male, % (n/N)	55.0 % (22/40)
Body mass index, kg/m² (n = 38)	
▪ Mean (SD)	24.7 (4.2)
▪ Median (range) [IQR]	24.2 (16.6 to 34.0) [21.6 to 27.9]
Etiology of chronic pancreatitis, % (n/N)	
▪ Alcohol	35.0 % (14/40)
▪ Idiopathic	57.5 % (23/40)
▪ Metabolic	2.5 % (1/40)
▪ Abnormal anatomy	2.5 % (1/40)
▪ Hereditary	2.5 % (1/40)
▪ Autoimmune	0.0 % (0/40)
Prior occurrence of chronic pancreatitis, % (n/N)	
▪ Pseudocysts	7.5 % (3/40)
▪ Downstream stenosis	10.0 % (4/40)
▪ Duodenal stenosis	0.0 % (0/40)
▪ Common bile duct narrowing	5.0 % (2/40)
▪ Weight loss	45.0 % (18/40)
Prior post-ERCP pancreatitis	5.1 % (2/39)
ASA category	
▪ I	25.0 % (10/40)
▪ II	50.0 % (20/40)
▪ III	25.0 % (10/40)
▪ IV	0.0 % (0/40)
▪ V	0.0 % (0/40)
Baseline MPD diameter before treatment, mm (n = 35)	
▪ Mean (SD)	8.4 (2.9)
▪ Median (range) [IQR]	8.0 (5.0 to 16.0) [6.0 to 10.0]
MPD stricture, % (n/N)	47.5 % (19/40)
Number of stones (n = 36)	
▪ Mean (SD)	1.7 (1.3)
▪ Median (range) [IQR]	1 (1 to 7) [1 to 2]
Mean (SD) stone size, mm	9.8 (3.5)

IQR, interquartile range; ERCP, endoscopic retrograde cholangiopancreatography; ASA, American Society of Anesthesiologists; MPD, main pancreatic duct.

in IPS and MPD diameter from baseline to 6-month follow-up was evaluated using a paired *t* test. *P* values < 0.05 were considered significant. All analyses were performed using SAS version 9.4.

Results

A total of 55 patients were consecutively screened for inclusion between February 2019 and June 2021, of whom 43 patients could be included in the study (▶ **Fig. 2**). Three patients were identified as screening failures, which left 40 patients for the primary end point analysis. Statistics were recalculated and 40 patients still provided a power of 79.4 % and it was therefore decided not to reopen enrollment. Completion of the primary end point was confirmed on the day after the procedure during the daily multidisciplinary board meeting in which patients who have had radiographs taken are discussed.

The patient demographic and baseline characteristics are shown in ▶ **Table 1**. The majority of patients (60 %; 24/40) had at least one stone located in the pancreatic head, while there were 12.5 % (5/40) with a stone located in the genu, and 35 % (14/40) with a stone in the corpus of the pancreas. A total of 53 procedures were performed. Patients received rectal NSAIDs for PEP prevention in 92.5 % of the procedures (49/53) and an MPD stent was placed in 88.7 % of the procedures (47/53).

Primary end point

EHL was used in 92.5 % of the DSOP procedures (49/53) and laser lithotripsy in 1.9 % (1/53). In two procedures, after dilation and visualization with DSOP, the stone could be mobilized enough for it to be flushed out or easily extracted with a basket. The intention-to-treat (ITT) analysis showed a 90 % success rate (36/40), which is statistically significantly higher than the performance goal of 74 % ($P = 0.01$). In the per-protocol analysis), CSC was achieved in 92.1 % (35/38; $P = 0.005$) (▶ **Table 2**).

Follow-up of 6 months was completed in 97.1 % of patients with successful CSC in the initial DSOP procedures (34/35), and none had residual stones left. CSC was established in 72.5 % (29/40) after the first procedure, in 7.5 % (3/40) after two procedures, and in 7.5 % (3/40) after three procedures. Endoscopic sphincterotomy, dilation, and DSOP were generally performed in one session. In one case, dilation was performed twice before DSOP, which was then performed successfully (third procedure). In this case, the two first attempts were counted as procedure failures. Out of the four treatment failures with DSOP, one patient underwent surgery (no cannulation and therefore ERCP with DSOP was not possible), and three patients had one DSOP and were then sent for ESWL. Conventional ERCP was performed after ESWL with CSC in all three cases.

Secondary end points

The mean (SD) baseline IPS was 55.3 (46.2). Overall pain relief at 6-month follow-up was achieved in 82.4 % of patients (28/34). Of these 28 patients, complete pain relief was reported in 61.8 % (21/34) and partial pain relief in 20.6 % (7/34). The de-

▶ **Table 2** Results for the primary end point showing significant technical success for stone clearance compared with extracorporeal shock wave lithotripsy.

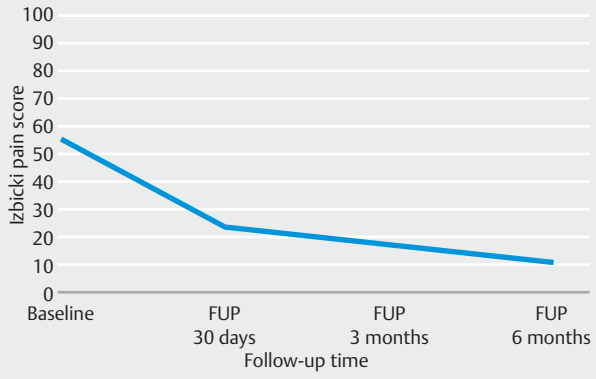
	Rate	Performance goal	Lower 95 % CI	*P* value
Complete stone clearance (ITT)	90.0 % (36/40)	74.0 %	76.3 %	0.01
Complete stone clearance (treated)	92.1 % (35/38)	74.0 %	78.6 %	0.005

ITT, intention to treat.

▶ **Table 3** Izbicki pain score over time in patients with symptomatic chronic pancreatitis and three or more main pancreatic duct stones who were treated by digital single-operator pancreatoscopy-guided lithotripsy.

	Izbicki pain score	Change in Izbicki pain score from baseline	*P* value
Baseline (n = 40)			
▪ Mean (SD)	55.3 (46.2)		
▪ Median (range) – [IQR]	49.5 (0.0 to 303.8) [33.5 to 63.8]		
Final 3-month visit (n = 34)			< 0.001
▪ Mean (SD)	17.3 (22.9)	−42.9 (47.3)	
▪ Median (range) – [IQR]	0.0 (0.0 to 76.3) [0.0 to 25.8]	−44.6 (−272.1 to 6.3) [−50.0 to −17.5]	
6-month visit (n = 34)			< 0.001
▪ Mean (SD)	10.9 (18.3)	−47.2 (48.3)	
▪ Median (range) – [IQR]	0.0 (0.0 to 76.3) [0.0 to 18.3]	−45.3 (−280.4 to 6.3) [−50.0 to −23.3]	

IQR, interquartile range.



▶ **Fig. 3** Line graph showing the Izbicki pain score constantly decreasing over the follow-up period.

tailed changes in the IPS over time are shown in ▶ **Table 3** and ▶ **Fig. 3**.

The mean (SD) number of interventions was 1.4 (0.6). The mean (SD) MPD diameter was significantly reduced from 8.4 (2.9; n = 35) to 4.9 (1.9; n = 35), resulting in an improvement of −3.7 (2.8; $P < 0.001$). It was possible to visualize the target stone in 96.2 % of the procedures (49/53) and a MPD stent was placed in 88.7 % of the procedures (47/53) either for strictures or for prophylactic reasons. In five procedures, stent placement was not performed because of complete duct clearance and there being no significant strictures. No PEP occurred after these procedures. The mean (SD) DSOP procedure time was 31.1 (19.0) minutes (n = 52).

SAEs

One patient had an intraprocedural bleed after sphincterotomy, but it was possible to treat this conservatively and it had no impact on the lithotripsy. SAEs were seen in 12.5 % of patients (5/40) and in 9.4 % of procedures (5/53). Two patients had a nonprocedure-related hospital admission: vertigo (n = 1), heart attack (n = 1). Two patients were admitted with an exacerbation of pain, probably due to stent dislocation. One patient had acute pancreatitis after stent dislocation. All of the SAEs occurred during follow-up and not during the procedure itself.

Discussion

The technical success rate for DSOP-guided therapy of PD stones in our study with persistent stone clearance after 6 months was high (92 %). This technical success rate was in line with findings from the literature (88 % to 100 %) [4, 5, 11, 17, 18]. Overall pain relief at 6-month follow-up was achieved in 82 % of patients after CSC and the MPD size, as an expression of ductal pressure, was significantly reduced from 8.4 mm to 4.9 mm. To date, no other prospective multicenter DSOP trials with 6-month follow-up and IPS assessment have been published. However, the results of our study are comparable with a recent ESWL trial (n = 5124), which reported CSC in 73 % of patients and pain relief in 83 % of patients after 6 months [19].

The decrease in IPS after 6 months was statistically significant compared with the results for combined complete and partial pain relief for the endoscopic groups in the studies of Cahen et al. (30 %) [20] and Issa et al. (39 %) [21]. Possible explanations for the high pain relief rates in our study are the experience of the endoscopists, the possibility of directly treating MPD stenoses, and the high technical success rate of DSOP. In addition, our cohort showed a difference in the population, having a higher proportion of women and a lower proportion of patients with alcohol-induced chronic pancreatitis compared with earlier trials [21, 22].

The treatment of stones with ESWL in chronic pancreatitis clearly has limitations. Effective ESWL is painful for patients and can therefore only be performed with strong analgesic therapy using either general or epidural anesthesia. Only a limited number of centers in Europe and the USA have direct access to a lithotripter or have their own ESWL machine. This makes planning of the procedure challenging and, depending on the faculty running the lithotripter (it is usually performed at a urology department), less effective. ESWL without subsequent ERCP is a successful treatment; however, in patients with MPD strictures and/or obstructing MPD stones, ESWL is often preceded by a (prior) ERCP [23]. This is supported by our own data from this study, which showed that subsequent stent therapy after lithotripsy was required in 88.7 % of procedures.

Compared with the previously published data on CSC with ESWL, our results show a promising success rate, without the need for epidural anesthesia, with a mean (SD) number of 1.4 (0.6) procedures. This includes the subsequent conventional ERCP, which can be performed during the same session of DSOP. Undergoing fewer procedures is important for patient comfort and may lead to lower costs. However, in both modalities further ERCP for stricture therapy may be necessary after CSC.

A randomized clinical trial comparing early surgery versus endoscopy showed higher complete or partial pain relief in the surgical group compared with those undergoing endoscopy (58 % vs. 39 %), but treatment effects reduced significantly during follow-up [21]. In the subgroup of endoscopically treated patients with complete duct clearance, the pain scores at 7 months were reported to be similar to the surgery cohort and were lower compared with the subgroup of patients with incomplete duct clearance. This indicates the importance and necessity of aiming for CSC. DSOP-guided lithotripsy can achieve substantial rates of complete duct clearance, namely in 92.1 % of patients in our study, and leads to a high rate of medium-term (6 months) pain relief. Chronic pancreatitis is an ongoing inflammatory disease, and it is still unclear if an invasive intervention such as surgery can indeed lead to long-term symptom relief, especially as surgical data show a high number of patients with persisting pain and drug dependance during long-term follow-up [8]. The significant change in the MPD after CSC is in line with the reduction of pain in this cohort. This underscores the importance of decompression as a key treatment goal in patients with chronic pancreatitis and MPD dilatation.

The proportion of SAEs in our study was lower than in previously published data, which might be explained by PEP pro-

phylaxis (PD stent and/or rectal NSAID), careful patient selection, and the growing experience in the field of DSOP-guided lithotripsy [4, 16]. In addition, stent dislocation during follow-up was also classified as an SAE, but was unlikely related to DSOP as a stent would also have been placed to resolve a stricture after conventional ESWL and ERCP. All SAEs were treated conservatively, with no mortality.

Our study has several strong points, including its prospective multicenter design, with predefined population selection, follow-up of at least 6 months, and clinically useful end points. However, there are also some limitations. First, we did not perform a prospective randomized controlled trial against the current golden standard (ESWL ± ERCP and/or surgery). Second, follow-up was at least 6 months but more information is needed on the sustained clinical effect of DSOP-guided lithotripsy. DSOP-guided treatment is a challenging procedure and the findings of our study may not be generalizable as procedures were performed by experienced endoscopists in tertiary referral centers. Third, no cost-effectiveness analysis was performed in which DSOP-guided lithotripsy was compared with the standard of care. Fourth, we enrolled 40 patients, which was fewer than the calculated required sample size of 43 patients and is fewer compared with the number of patients reported in evaluations of ESWL. However, our technical success rate of DSOP of 92 % was well above the 74 % with ESWL, as reported in previous studies ($P = 0.005$) (▶ **Table 2**).

In conclusion, DSOP-guided lithotripsy for large symptomatic PD stones was shown to be technically and clinically successful, safe, and can be a promising endoscopic addition or alternative to ESWL combined with ERCP in this highly selected group of patients. DSOP is a challenging technique and should be performed in centers with a multidisciplinary team experienced in pancreatic pathology and its management. Further studies comparing against the standard of care and with larger groups of patients, evaluating outcome and cost-effectiveness, are needed to define the role of DSOP in the treatment algorithm of patients with chronic pancreatitis.

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Competing interests

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CORRECTION

Digital single-operator pancreatoscopy for the treatment of symptomatic pancreatic duct stones: a prospective multicenter cohort trial

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In the above-mentioned article, the authors of the working group have been included. This was corrected in the online version on August 26, 2022.

In the above-mentioned article, one sentence in the Abstract, Section Method was corrected. Correct is: Patients with symptomatic chronic pancreatitis and three or fewer stones ≥ 5mm in the main pancreatic duct (MPD) of the pancreatic head or body were included. This was corrected in the online version on February 26, 2023.