Long-term outcomes associated with pancreatic extracorporeal shock wave lithotripsy for chronic calcific pancreatitis

Gulseren Seven, MD,[1] Mitchal A. Schreiner, MD, MPH,[1] Andrew S. Ross, MD,[1] Otto S. Lin, MD,[1] Michael Gluck, MD,[1] S. Ian Gan, MD,[1] Shayan Irani, MD,[1] John J. Brandabur, MD,[1] David Patterson, MD,[1] Christian Kuhr, MD,[2] Richard Kozarek, MD[1]

Seattle, Washington, USA

Background: Most outcomes data on pancreatic extracorporeal shock wave lithotripsy (P-ESWL) for chronic calcific pancreatitis (CCP) are based on studies with <4 years' follow-up, and U.S. long-term studies are lacking.

Objective: To report long-term P-ESWL outcomes for CCP and to assess whether smoking or alcohol use influences P-ESWL outcomes.

Design: Cross-sectional study, retrospective chart review.

Setting: Virginia Mason Medical Center, Seattle, Washington.

Patients: This study involved 120 patients who underwent P-ESWL and ERCP for CCP and completed an outcomes questionnaire.

Intervention: P-ESWL and ERCP, outcomes survey.

Main Outcome Measurements: Pain, quality of life, narcotics use, diabetes status, pancreatic enzyme requirement, repeat P-ESWL, repeat ERCP, surgery.

Results: A total of 120 patients underwent P-ESWL followed by ERCP (mean ± standard deviation [SD] follow-up 4.3 [± 3.7] years) and completed a survey. The mean (± SD) before-P-ESWL pain score was 7.9 (± 2.6) compared with 2.9 (± 2.6) after P-ESWL ($P < .001$). Improved pain was reported by 102 patients (85%); 60 (50%) reported complete pain relief and no narcotic use. The mean (± SD) before-P-ESWL quality-of-life score was 3.7 (± 2.4) compared with 7.3 (± 2.7) after P-ESWL ($P < .001$). In patients with ≥4 years' follow-up, repeat procedures included P-ESWL (29%), ERCP (84%), and surgery (16%). Smokers who quit smoking after P-ESWL had improved narcotic requirements compared with those who continued smoking (95% vs 67%; $P = .014$), and a trend suggested a decreased need for repeat ERCPs (68% vs 84%; $P = .071$).

Limitations: Single center, retrospective, recall bias, nonvalidated pain and quality-of-life scales.

Conclusion: P-ESWL as the initial therapy for CCP may lead to more lifetime procedures; however, partial pain relief in 85%, complete pain relief with no narcotic use in 50%, and avoidance of surgery in 84% of patients may be achieved. Quitting smoking after P-ESWL may improve outcomes. (Gastrointest Endosc 2012;75:997-1004.)

In 2002 our group reported the results of an analysis on the outcomes of 40 patients who underwent pancreatic extracorporeal shock wave lithotripsy (P-ESWL) for chronic calcific pancreatitis (CCP), with a mean follow-up of 2.4 years.[1] Our 2002 analysis revealed a statistically significant improvement in pain scores, hospital admissions, and narcotic pain

Abbreviations: CCP, chronic calcific pancreatitis; P-ESWL, pancreatic extracorporeal shock wave lithotripsy; PD, pancreatic duct.

DISCLOSURE: *This study received live course support and live endoscopy course support from Olympus America, Boston Scientific Corporation, and Cook Medical as well as equipment donation to the Virginia Mason Medical Center. No other financial relationships relevant to this publication were disclosed.*

0016-5107/$36.00

doi:10.1016/j.gie.2012.01.014

Received June 27, 2011. Accepted January 9, 2012.

Current affiliations: The Digestive Disease Institute at Virginia Mason (1), Department of Urology (2), Virginia Mason Medical Center, Seattle, Washington, USA.

Reprint requests: Richard A. Kozarek, MD, Executive Director, Digestive Disease Institute, Virginia Mason Medical Center, 1100 9th Ave, PO Box 900, Mail Stop C3-GAS, Seattle, WA 98101.

medication use in patients who underwent this therapy. A number of studies on this same subject have also noted improvements in pain, quality of life, narcotic pain medication use, and pancreatic duct (PD) diameter.[2-13] In 2007, Cahen et al[14] published a randomized, prospective, head-to-head trial reporting superior outcomes associated with surgical drainage, compared with endoscopic drainage, of the PD in chronic pancreatitis. The majority of the patients in both arms of that study had PD stones, so the findings of this study have largely been applied to patients with CCP with intraductal stones.

Despite the results of the Cahen et al[14] study, which reported surgical drainage of the PD in chronic pancreatitis to be superior to endoscopic drainage, because of the positive outcomes associated with P-ESWL in the treatment of CCP reported at our institution and others,[1-13] P-ESWL remains an important tool for the treatment of these patients and warrants continued study. Although a wealth of data exists on after–P-ESWL outcomes, current data are based largely on studies with <4 years of follow-up, and studies based on U.S. patients are lacking. The primary aim of this study was to assess the long-term clinical outcomes associated with P-ESWL for CCP. The secondary aim was to evaluate whether or not smoking cigarettes or daily alcohol use influences P-ESWL outcomes.

Take-home Message

- In long-term follow-up after pancreatic extracorporeal shock wave lithotripsy (P-ESWL) for chronic calcific pancreatitis with intraductal stones, 85% of patients achieved at least partial pain relief, 50% of patients achieved complete pain relief with no narcotic use, and 84% avoided pancreas surgery.
- Cigarette smokers who quit smoking after P-ESWL required less narcotic medication after P-ESWL, and a trend suggested less need for follow-up ERCPs than in those who continued to smoke.

METHODS

All patients who underwent P-ESWL followed by ERCP for CCP between January 1, 1990 and November 1, 2010 at the Virginia Mason Medical Center were included. The social security death index was used to exclude all patients who were no longer living. A questionnaire was then mailed to all after–P-ESWL patients who were still living in order to collect outcomes data for measurement (Appendix, available online at www.giejournal.org). The questionnaire contained before–P-ESWL and after–P-ESWL ordinal pain and quality-of-life scale scores as well as questions on before and after P-ESWL narcotic pain medication use, cigarette smoking status (daily cigarette use), alcohol use (at least one alcoholic drink per day), diabetes status, and pancreatic enzyme supplement requirement. Both the ordinal pain and quality-of-life scales were based on a scale of 1 to 10. For the pain scale, 1 represented no pain, and 10 represented maximal pain. For the quality of life scale, 1 represented the lowest quality of life, and 10 represented the best quality of life. A section at the top of the questionnaire allowed participants to opt out of the study by checking a box and returning the survey uncompleted. If a participant did not opt out of the study within 1 month after receiving the questionnaire, consent to be contacted by telephone to complete the survey was implied if they had not already returned a completed questionnaire. A retrospective chart review was then performed on all patients who had completed a questionnaire either by mail or telephone to collect data regarding the need for follow-up procedures after the initial P-ESWL and ERCP, including repeat P-ESWL, repeat ERCP, and pancreas surgery. Additional review included demographic features, etiology of CCP, and surgical status of patients who were excluded from the study.

For our secondary analysis, we set out to determine whether cigarette smoking or daily alcohol use had an influence on our after–P-ESWL outcomes, including improvement in before and after P-ESWL pain scale scores, quality-of-life scale scores, and narcotic pain medication use as well as the percentage of patients who reported no pain and no narcotics use and the need for repeat P-ESWL, ERCP, and pancreas surgery. For smoking, we compared the following groups: (1) no smoking history versus smoking history either before P-ESWL or at present, (2) no smoking history versus prior smokers who quit after P-ESWL, (3) no smoking history versus prior smokers who were still smoking, and (4) prior smokers who quit after P-ESWL versus prior smokers who were still smoking. For alcohol use, we compared the following groups: (1) no daily alcohol use history versus daily alcohol use history either before P-ESWL or currently, (2) no daily alcohol use history versus participants with daily alcohol use before P-ESWL but who quit after P-ESWL, (3) no daily alcohol use history versus participants with daily alcohol use before P-ESWL who still used alcohol daily, and (4) participants with daily alcohol use before P-ESWL who quit after P-ESWL versus participants with daily alcohol use before P-ESWL who still used alcohol daily.

Before October 2008, P-ESWL was performed at our institution with a Dornier HM3 lithotripter (Dornier, Inc, Dornier Medtech, Munich, Germany), as previously described.[1] In October 2008, we began performing P-ESWL with a Storz Medical Modulith SLX-F2 lithotripter (Karl Storz Lithotripsy America, Inc, Kennesaw, Ga), and fragmentation was accomplished with a mean of 2312 (range 1400-3000) cycles with a mean maximum energy of 7.5 (range 6.5-8) joules. All procedures were performed with patients under general anesthesia. Two-thirds of the patients underwent ERCP immediately after P-ESWL, and one-third of the patients underwent ERCP the following day. Delaying P-ESWL for 24 hours resulted in an increased need for pain medication after P-ESWL and before

undergoing subsequent ERCP. Criteria to perform P-ESWL in our institution are stones larger than 5 to 10 mm, with a marked discrepancy in size of stone versus downstream PD that would preclude stone removal without significant fragmentation. The discrepancy in size between the stones and downstream PD was assessed by cross-sectional imaging (CT scan alone and/or MRCP). Although fragmentation is somewhat subjective, it is considered successful when the stones appear smaller in size and/or less dense on fluoroscopy as assessed by the treating urologist. A good result can be observed when stone fragments start to back-fill the PD on fluoroscopy. Repeated sessions of P-ESWL are required in patients with incomplete fragmentation relative to downstream duct diameter on successive days until fragmentation is achieved.

All patients had one or more of the following complaints: recurrent bouts of pancreatitis or ongoing chronic pain despite escalating use of analgesics. Patients referred for surgical evaluation included younger patients, those with PDs dilated to 7 to 8 mm or more, and those with failure of endotherapy defined by one or more of the following: refractory pain, relapsing pancreatitis, or failure to maintain patency of a stricture despite up to 2 years of maximal endotherapy. After P-ESWL, patients underwent ERCP within 48 hours. All patients were treated with major and/or minor papilla sphincterotomies contingent on dominant anatomy and stone burden. Strictures were balloon dilated, and stone fragments were removed with balloon and basket technology as well as saline solution irrigation of stone fragments from PD side branches. In patients with a large residual stone burden, a Soehendra screw extractor (Cook Inc., Winston-Salem, NC) was used over a guidewire to assure the ability to place a PD endoprosthesis. Patients without residual stones or high-grade strictures had small-caliber (3-5F) prostheses placed in anticipation of spontaneous passage. Patients with significant residual stone burdens as well as those with high-grade strictures had 1 to 2, 7F PD stents placed in anticipation of repeat endoscopic therapy several months later.

SPSS Statistics 18.0 software was used. Before versus after P-ESWL nominal data were analyzed by using a chi-square test, and continuous data were analyzed with the *t* test. The Wilcoxon signed-rank test was used to compare our ordinal before– versus after–P-ESWL pain scale and quality-of-life data. Statistics are reported as means with standard deviation (SD) as the measure of variance.

RESULTS

Total P-ESWL population

Within our study period, 215 patients (112 male, 103 female; mean [± SD] age 53 [± 15] years; range 11-90 years) underwent P-ESWL followed by ERCP at our institution. The median time between diagnosis of CCP and initiation of therapy was 63 months (range 1-420 months). Alcohol was the dominant cause in 118 (55%) of 215 patients. Other causes were idiopathic CCP in 67 patients, hereditary pancreatitis in 19 (concomitant alcohol use in 3), hypercalcemia in 5 (3 chronic renal failure, 2 hyperparathyroidism), and history of trauma in 4 (concomitant alcohol use in 2). Additional etiologies included anastomotic surgical strictures with upstream stones in 4 patients (3 Whipple procedures, 1 for cystadenoma of pancreas, 1 for a retained metal biliary stent placed percutaneously and cholangitis, 1 for ampullary cancer, and 1 surgical sphincteroplasty of the PD and choledochoduodenostomy for duodenal perforation after biliary sphincterotomy), congenital abnormal pancreaticobiliary junction in 2, hyperlipidemia in 1 (concomitant alcohol use), and celiac disease in 1. Eleven patients had pancreas divisum, 3 of whom were classified as related to alcohol, 3 with hereditary pancreatitis, and 5 in the idiopathic group. Presentation included severe chronic abdominal pain in 104 patients, relapsing bouts of pancreatitis in 68, one episode of severe acute pancreatitis in 24, and moderate pain in conjunction with steatorrhea in 19. Multiple patients had 2 or more of these symptoms.

Surveyed patients

A total of 177 patients were still living, and 2 of those were excluded due to prior pancreas surgery. We therefore sent out questionnaires to 175 patients and were able to get completed surveys on 120 patients, for a 68% survey completion rate (Fig. 1). Within this cohort, the mean (± SD) age was 52 (± 15) years (range 11-88 years), and there were 68 female (57%) and 52 male (43%) patients (Table 1). Eighty-five patients (71%) reported smoking cigarettes before undergoing P-ESWL, and 53 (44%) continued to smoke. Sixty-six patients (55%) reported drinking at least one alcoholic drink per day before undergoing P-ESWL, and 10 (8%) continued to drink at least one alcoholic drink per day. The mean (± SD) follow-up was 4.3 (± 3.7) years.

Of the 120 patients who returned surveys, 92 (77%) had multiple calculi, and 28 (23%) had a single stone (mean maximum diameter 14 mm, range 5-25 mm). Stones were present in the head of the pancreas in 80 patients, head and body in 2, body alone in 3, and in head, body, and tail in 35. Concomitant pancreas pathology noted at ERCP included dominant PD stricture in 64 patients (53%), duct leakage in 8 (7%), and pseudocysts in 15 (12%). Stenting was performed in 114 patients (95%); 72 (63%) had 1 stent, and 42 (37%) had 2 stents.

Comparing before– versus after–P-ESWL pain scores, the mean (± SD) before–P-ESWL pain score was 7.9 (± 2.6) compared with 2.9 (± 2.6) in after–P-ESWL patients ($P < .001$) (Table 2). There was an improvement in the before– versus after–P-ESWL pain scale scores in 102 patients (85%), a worsening of pain in 4 patients (3%), and unchanged pain scale scores in 14 patients (12%) ($P < .001$). Complete pain relief (pain scale score of 1) was reported in 61 patients (51%) after P-ESWL. Of the 91

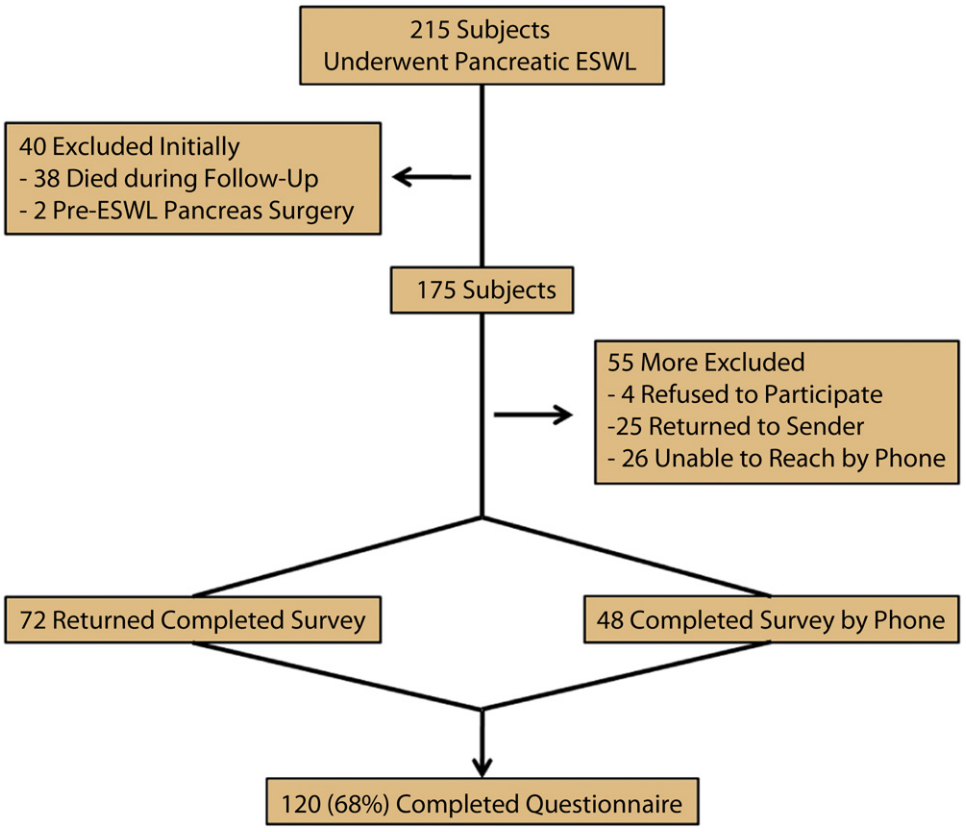

Figure 1. Study enrollment. *ESWL,* extracorporeal shock wave lithotripsy.

TABLE 1. Patient characteristics (N = 120)

Age, no. (%), y	52 (15)
Age range, no., y	11-88
Female, no. (%)	68 (57)
Male, no. (%)	52 (43)
Cigarette smoking before pancreatic ESWL, no. (%)	85 (71)
Current cigarette smoking, no. (%)	53 (44)
Daily alcohol use before pancreatic ESWL, no. (%)	65 (54)
Current daily alcohol use, no. (%)	10 (8)
Follow-up period, mean (SD), y	4.3 (3.7)

ESWL, Extracorporeal shock wave lithotripsy; *SD,* standard deviation.

TABLE 2. The results of before–P-ESWL and after–P-ESWL for pain score, quality-of-life score, diabetes, and pancreatic enzyme requirement

	Before P-ESWL	After P-ESWL	*P* value
Pain score, mean (SD)	7.9 (2.6)	2.9 (2.6)	< .001
Quality-of-life score, mean (SD)	3.7 (2.4)	7.3 (2.7)	< .001
Presence of diabetes, no. (%)	22 (18)	42 (35)	< .001
Pancreatic enzyme requirement, no. (%)	63 (53)	65 (54)	= .758

ESWL, Extracorporeal shock wave lithotripsy; *SD,* standard deviation.

patients taking narcotics for pain before undergoing P-ESWL, 69 (76%) reported a decrease, 9 (10%) reported an increase, and 13 (14%) reported no change in their narcotic pain medication use after P-ESWL. Fifty-eight percent of patients taking narcotic pain medications before P-ESWL were able to discontinue narcotic pain medications after P-ESWL. Complete pain relief and no narcotic pain medication use were reported by 60 patients (50%) after P-ESWL. Looking at before– versus after–P-ESWL quality-of-life scores, the mean (± SD) before–P-ESWL quality-of-life score was 3.7 (± 2.4) compared with 7.3 (± 2.7) in after–P-ESWL patients ($P < .001$) (Table 2). There was an improvement in the before versus after P-ESWL quality-of-life scale scores in 93 patients (77%), a worsening of quality-of-life scores in 7 patients (6%), and no change in quality-of-life scores in 20 patients (17%) ($P < .001$). Twenty-two patients (18%) reported having diabetes before undergoing P-ESWL, and 42 patients (35%) reported having diabetes at present ($P < .001$). Sixty-three

TABLE 3. Comparison of outcomes between after-pancreatic ESWL patients needing no surgery with ≥4 years of follow-up and postsurgery patients

	Post-pancreatic ESWL patients needing no surgery with ≥4 years of follow-up (n = 44)	Post-pancreas surgery patients (n = 14)	*P* value
Repeat pancreatic ESWL, no. (%)	12 (27)	1 (7)	.116
Repeat ERCP, no. (%)	36 (82)	6 (43)	.004
Before-procedure pain scale, mean (SD)	8.2 (2.6)	8.8 (1.4)	.856
Improvement in pain scale, no. (%)	38 (86)	12 (86)	.951
After-procedure pain scale, mean (SD)	2.4 (2.3)	4.1 (3.1)	.032
Improvement in narcotic use (among patients treated with narcotics before initial pancreatic ESWL)	78% (25/32)	77% (10/13)	.930
Patients currently with no pain and no narcotic use, no. (%)	27 (61)	3 (21)	.009
Quality-of-life before procedure, mean (SD)	3.2 (2.3)	3.5 (2.2)	.529
Quality-of-life improvement, no. (%)	37 (84)	9 (64)	.111
Quality-of-life after the procedure, mean (SD)	7.5 (2.7)	6.7 (2.6)	.321

ESWL, Extracorporeal shock wave lithotripsy; *SD,* standard deviation.

patients (53%) reported using pancreatic enzyme supplements before undergoing P-ESWL, and 65 patients (54%) reported using pancreatic enzyme supplements at present ($P = .758$) (Table 2).

For our repeat procedures analysis, we chose to look only at patients who had at least 4 years of follow-up. This cohort consisted of 55 patients with a mean (± SD) follow-up of 7.5 (± 3.0) years. Sixteen patients (29%) required repeat P-ESWL, with a mean number of repeat P-ESWL procedures of 0.33 (range 0-2). Eight patients required a second P-ESWL within the first 6 months to complete stone fragmentation, and 8 additional patients underwent a second lithotripsy for recurrent calculus at a mean (± SD) of 31 (± 20) months (range 7-64 months). Forty-six patients (84%) required at least one repeat ERCP after the initial P-ESWL and ERCP, with a mean (± SD) number of repeat ERCP procedures of 2.5 (± 2.5) (range 0-12). Finally, 9 patients (16%) with at least 4 years of follow-up ultimately required pancreas surgery for their CCP. Two additional patients underwent pancreas surgery for intraductal papillary mucinous neoplasm and islet cell tumor.

We also compared patients with ≥4 years of follow-up who did not undergo pancreas surgery (n = 44) to all patients who underwent pancreas surgery during our follow-up period (n = 14). There was a mean (± SD) time of 24 (± 15) months (range 2-56 months) between ESWL and surgery. Ten patients had Whipple procedures, 3 had distal pancreatectomies, and 1 had a Puestow procedure. Indications of surgery for their CCP included one or a combination of the following: recurrent attacks of pancreatitis (n = 2), multiple stones (n = 6), and pain (n = 6) in spite of multiple interventions, high-grade PD stricture (n = 7), PD stent dependence (n = 3), impacted stone in a papilla (n = 1), and pancreatic necrosis and pseudocysts in the tail of the pancreas (n = 1). There was a mean (± SD) time of 45 (± 42) months (range 1-128 months) after surgery. There was not a statistically significant difference in the percentage of patients requiring follow-up P-ESWL in the nonsurgery group versus the postsurgery group (27% vs 7%, respectively; $P = .115$). However, the number of patients requiring repeat ERCP was significantly higher in the nonsurgery group versus the postsurgery group (82% vs 43%, respectively; $P = .004$). Table 3 includes our comparison of both repeat procedures and clinical symptoms between the nonsurgery patients with ≥4 years of follow-up and the postsurgery patients. ERCP was performed in 5 patients who had undergone pancreatic surgery for CCP. The indications for ERCP were pain in 3 patients and relapsing pancreatitis in 2. Endoscopic findings included multiple stones and stenotic anastomosis in 3 patients, a migrated stent in 1 patient, and a stricture in the head of the pancreas in 1 patient who underwent distal pancreatectomy. Statistically significant differences between the two groups in the after–P-ESWL symptom outcomes included a lower mean (± SD) current pain scale score (2.4 ± 2.3 versus 4.1 ± 3.0; $P = .032$) and a greater percentage of patients who currently reported both no pain (score of 1 on pain scale) and no narcotics (61% vs 21%; $P = .009$) in the nonsurgery group.

Four of 44 patients (9%) with at least 4 years of follow-up still require pancreatic stenting at present. Five patients experienced clinically significant biliary stricture, and pseudocysts were observed in 3 patients. Biliary strictures were managed endoscopically. Of the 5 patients, 1 required a subsequent Whipple procedure because of failure of P-ESWL, pancreatic duct stricture, and retained stones; 3 have been successfully treated with plastic or covered metal stents; and 1 was lost to follow-up. Pseudocysts were spontaneously resolved in 1 patient, and the remaining 2 patients required endoscopic transduodenal drainage and surgery.

Our extensive analysis to determine whether cigarette smoking or daily alcohol use had an effect on our after–P-ESWL outcomes revealed only one statistically significant difference. We found that narcotic pain medication use was significantly improved among patients who were smokers before undergoing P-ESWL but quit after P-ESWL, compared with patients who were smokers before undergoing P-ESWL and continued to smoke (95% vs 67%, respectively; $P = .014$). Between these same two groups, we also noted a trend suggesting a decreased need for repeat ERCPs in favor of those who were smokers before undergoing P-ESWL but have since quit smoking (68% vs 84%; $P = .071$). There were no other statistically significant findings or trends (with a P value $< .100$) in the after–P-ESWL outcomes between the two groups or any of the other cigarette smoking or daily alcohol use analyses.

DISCUSSION

The findings in the present study fit into the current body of literature on P-ESWL for the treatment of CCP with intraductal stones in a number of ways. One, our study adds to the literature showing P-ESWL to be an effective treatment modality for CCP. Two, the present study suggests that the positive outcomes noted in our initial analysis performed in 2002 are durable, because our initial positive outcomes have persisted. Finally, we have found that patients who quit smoking after P-ESWL may see improved outcomes.

The positive long-term outcomes reported in our study are comparable to outcomes reported in the great majority of studies on P-ESWL for CCP. Our study reported that at least partial pain relief occurred in 85% of patients, and complete pain relief with no need for narcotic pain medications occurred in 50% of patients. An after–P-ESWL study by Tandan et al[11] with a very large cohort (n = 1006) reported that 84% of the patients who returned for follow-up at 6 months noted a significant relief of pain with a decrease in analgesic use. In 2.2 years of follow-up after P-ESWL for CCP, Costamagna et al[6] reported that 72% of patients did not have a relapse in pain. In a study of 123 patients with a mean follow-up of 1.2 years, Delhaye et al[3] reported at least partial pain relief in 85% and complete pain relief in 40% of patients who underwent P-ESWL for CCP. The same group later published a long-term outcomes study[10] with a mean follow-up of 14.4 years and reported a clinical success rate (defined as ≤5 hospitalizations for pain during the total follow-up period and no surgery) of 66%. An after–P-ESWL study by Adamek et al[7] reported considerable or complete pain relief in 76% of patients, and 43% of patients did not require analgesics after P-ESWL, with a mean follow-up period of 3.3 years. Another long-term follow-up, after–P-ESWL study by Tadenuma et al,[12] with a mean follow-up period of 6.5 years, noted that 63% of their patients never experienced a relapse in pain during follow-up. A multicenter study by Inui et al[13] reported that 91% of 555 patients from 11 institutions had relief from their pain. Finally, prospective trials by Sauerbruch et al[4] and Brand et al[8] regarding P-ESWL for CCP reported at least partial pain relief in 88% and 82% of patients, respectively, and considerable or complete pain relief in 50% and 45% of patients, respectively.

Because we analyzed our patients on an intention-to-treat basis, our study findings may be compared with the endoscopic treatment arm in the Cahen et al[14] study. The findings in our study differed from those of the patients randomized to the endoscopic treatment arm in that study in that our after–P-ESWL patients had a greater rate of at least partial pain relief (85%, 102/120 vs 32%, 6/19, respectively) and complete pain relief (51%, 61/120 vs 16%, 3/19, respectively). The discrepancies in outcomes seen between our studies may be related to a number of factors, including the following: (1) inherent differences in lithotripters or P-ESWL technique as well as endotherapy techniques, (2) a much larger cohort in our study, and (3) a mean follow-up period of 4.3 years in our study, compared with a total follow-up time of 2 years in the Cahen et al[14] study. When making these comparisons, we do not take lightly the fact that the Cahen et al study was a randomized, prospective trial, and our study is based on data obtained from a retrospective chart review and a survey that required patients to report on clinical information that, in many cases, dated back several years. These authors have subsequently published a longer-term follow-up of the original cohort, randomized to surgery or endoscopic treatment, and have confirmed increased efficacy of surgery when compared with P-ESWL and ERCP.[15]

In the initial after–P-ESWL study performed at our institution,[1] with a mean follow-up of 2.4 years, 20% (8/40) of patients required pancreas surgery. Among patients in the present study, with at least 4 years of follow-up and a mean follow-up of 7.5 years, the percentage of patients who ultimately required surgery remained at 16% (9/55) and 20% (11/55) for all of indications. The long-term after-P-ESWL study by Delhaye et al,[10] reported that 21% of their patients required pancreas surgery. In the Cahen et al[14] study, 21% of patients randomized to the endoscopic therapy arm had their treatment converted to surgery. Other studies have reported after–P-ESWL surgery rates ranging from 4% to 13%.[5,7,9,13] Eight patients who were

excluded from the study required pancreatic surgery, and indication for surgery was inadequate CCP therapy in 4 of 8 patients. Twenty-two of 215 patients (10%) required pancreatic surgery, and CCP was the main indication for surgery in 16 of these patients (7%).

As stated in Methods, it is important to note that it is our institutional practice to perform ERCP after P-ESWL in all cases. We realize that the performance of ERCP immediately after P-ESWL is not universal practice, based largely on the findings in the Dumonceau et al[16] study, which reported that combining ERCP with P-ESWL did not improve the outcome of pancreatic pain. Along that same line, however, the study by Dumonceau et al would suggest that those who do not perform ERCP after P-ESWL can apply the findings of this study to their patients because similar results were seen between patients in their study who underwent ERCP after P-ESWL and those who did not. Because most patients underwent additional endoscopic therapy such as sphincterotomy and stenting, the treatment stratification relative to outcomes proved difficult. Despite a previous study, in which the authors found differences in shock wave characteristics for urinary stones between the two lithotripters used in the current study,[17] the investigators noted no significant difference in response to stone fragmentation and outcomes.

We found it interesting that 54% of patients reported drinking alcohol at least once a day, and 71% reported smoking cigarettes before undergoing P-ESWL for CCP, and now only 8% report continued use of alcohol, whereas 44% continue to smoke cigarettes. We think that the relatively high percentage of after–P-ESWL patients who continue to smoke compared with using alcohol may suggest that, although alcohol use has long been associated with chronic pancreatitis,[17] data showing smoking to be an independent risk factor for the development of chronic pancreatitis[18-25] have lagged. This has influenced the way we counsel our patients after P-ESWL for CCP, and, as a result, we have only more recently been stressing the link between smoking and CCP to our patients. It has been shown that cigarette smoking increases the risk of developing pancreas calcifications in patients with both alcoholic[26] and nonalcoholic[27,28] chronic pancreatitis. In the long-term P-ESWL outcomes study by Delhaye et al,[10] they made note of the fact that absence of smoking reported at the last follow-up evaluation was associated with improved long-term clinical success. Similarly, in our study, we found that smokers who quit smoking after P-ESWL required less narcotic pain medication after P-ESWL, and a trend suggested less of a need for follow-up ERCPs compared with those who continued to smoke.

There are several limitations to our study; however, the greatest limitation is that our results are based not only on a retrospective chart review but also a patient survey that introduced recall bias into our study. An additional limitation was use of nonvalidated pain and quality-of-life scales.

We conclude, however, based on the durable, positive, long-term outcomes in this study, that it remains reasonable to first attempt P-ESWL in the treatment of CCP with pancreatic duct stones. Although following this approach may lead to a patient requiring more lifetime procedures compared with those who proceed immediately to pancreas surgery, we have shown that when starting with P-ESWL, in long-term follow-up, one can expect to achieve at least partial pain relief in 85% of patients and complete pain relief with no narcotic use in 50% of patients, and pancreas surgery can be avoided in 84% of patients.

REFERENCES

1. Kozarek RA, Brandabur JJ, Ball TJ, et al. Clinical outcomes in patients who undergo extracorporeal shock wave lithotripsy for chronic calcific pancreatitis. Gastrointest Endosc 2002;56:496-500.
2. Cremer M, Vandermeeren A, Delhaye M. Extracorporeal shock wave lithotripsy (ESWL) for pancreatic stones. Gastroenterology 1988;94:A80.
3. Delhaye M, Vandermeeren A, Baize M, et al. Extracorporeal shock-wave lithotripsy. Gastroenterology 1992;102:610-20.
4. Sauerbruch T, Holl J, Sackmann M, et al. Extracorporeal lithotripsy of pancreatic stones in patients with chronic pancreatitis and pain; a prospective follow up study. Gut 1992;33:969-72.
5. Schneider HT, May A, Benninger J, et al. Piezoelectric shock wave lithotripsy of pancreatic duct stones. Am J Gastroenterol 1994;89:2042-8.
6. Costamagna G, Gabbrielli A, Massimiliano M, et al. Extracorporeal shock wave lithotripsy of pancreatic stones in chronic pancreatitis: immediate and medium-term results. Gastrointest Endosc 1997;46:231-6.
7. Adamek HE, Jakobs R, Buttmann A, et al. Long term follow up of patients with chronic pancreatitis and pancreatic stones treated with extracorporeal shock wave lithotripsy. Gut 1999;45:402-5.
8. Brand B, Kahl M, Sidhu S, et al. Prospective evaluation of morphology, function, and quality of life after extracorporeal shockwave lithotripsy and endoscopic treatment of chronic calcific pancreatitis. Am J Gastroenterol 2000;95:3428-38.
9. Farnbacher MJ, Schoen C, Rabenstein T, et al. Pancreatic duct stones in chronic pancreatitis: criteria for treatment intensity and success. Gastrointest Endosc 2002;56:501-6.
10. Delhaye M, Arvanitakis M, Verset G, et al. Long-term clinical outcome after endoscopic pancreatic ductal drainage for patients with painful chronic pancreatitis. Clin Gastroenterol Hepatol 2004;2:1096-106.
11. Tandan M, Reddy DN, Santosh D, et al. Extracorporeal shock wave lithotripsy and endotherapy for pancreatic calculi—a large single center experience. Indian J Gastroenterol 2010;29:143-8.
12. Tadenuma H, Ishihara T, Yamaguchi T, et al. Long-term results of extracorporeal shockwave lithotripsy and endoscopic therapy for pancreatic stones. Clin Gastroenterol Hepatol 2005;3:1128-35.
13. Inui K, Tazuma S, Yamaguchi T, et al. Treatment of pancreatic stones with extracorporeal shock wave lithotripsy. Pancreas 2005;30:26-30.
14. Cahen DL, Gouma DJ, Yung N, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic calcific pancreatitis. N Engl J Med 2007; 356:676-84.
15. Cahen DL, Gouma DJ, Laramee P, et al. Long-term outcomes of endoscopic vs surgical drainage of the pancreatic duct in patients with chronic pancreatitis. Gastroenterology 2011;141:1690-5.
16. Dumonceau JM, Costamagna G, Tringali A, et al. Treatment for painful calcified chronic pancreatitis: extracorporeal shock wave lithotripsy versus endoscopic treatment: a randomised controlled trial. Gut 2007;56: 545-52.
17. Zehnder P, Roth B, Birkhauser F, et al. A prospective randomised trial comparing the modified HM3 with the MODULITH® SLX-F2 lithotripter. Eur Urol 2011;59:637-44.

18. Durbec JP, Sarles H. Multicenter survey of the etiology of pancreatic diseases: relationship between the relative risk of developing chronic pancreatitis and alcohol, protein and lipid consumption. Digestion 1978;18:337-50.
19. Yadav D, Hawes R, Brand R, et al. Alcohol consumption, cigarette smoking, and the risk of recurrent acute and chronic pancreatitis. Arch Intern Med 2009;169:1035-45.
20. Lin Y, Tamakoshi A, Hayakawa T, et al. Cigarette smoking as a risk factor for chronic pancreatitis: a case-control study in Japan. Pancreas 2000; 21:109-14.
21. Talamini G, Bassi C, Falconi M, et al. Cigarette smoking: an independent risk factor in alcoholic pancreatitis. Pancreas 1996;12:131-7.
22. Bourliere M, Barthet M, Berthezene P, et al. Is tobacco a risk factor for chronic pancreatitis and alcoholic cirrhosis? Gut 1991;32: 1392-5.
23. Lowenfels AB, Zwemer FL, Jhangiani S, et al. Pancreatitis in a native American Indian population. Pancreas 1987;2:694-7.
24. Tolstrup JS, Kristiansen L, Becker U, et al. Smoking and risk of acute and chronic pancreatitis among women and men. Arch Intern Med 2009; 169:603-9.
25. Yen S, Hsieh CC, MacMahon B. Consumption of alcohol and tobacco and other risk factors for pancreatitis. Am J Epidemiol 1982;116:407-14.
26. Morton C, Klatsky AL, Udaltsova N. Smoking, coffee, and pancreatitis. Am J Gastroenterol 2004;99:731-8.
27. Cavallini G, Talamini G, Vaona B, et al. Effect of alcohol and smoking on pancreatic lithogenesis in the course of chronic pancreatitis. Pancreas 1994;9:42-6.
28. Imoto M, DiMagno EP. Cigarette smoking increases the risk of pancreatic calcification in late-onset but not early-onset idiopathic chronic pancreatitis. Pancreas 2000;21:115-9.

APPENDIX

☐ I do NOT wish to participate (If you do not wish to participate, please do one of the following:
1. Check this box and return this form to us in the enclosed envelope; 2. Send me an email at Mitchal.Schreiner@vmmc.org indicating you do not wish to participate; OR 3. Call and leave me a message at toll free (800)354-9527 ext 62791 indicating you do not wish to participate).

☐ I am willing to participate. (If you are willing to participate, please answer the following 16 questions and return this form to us in the enclosed envelope. Please fill out questions on both pages of the questionnaire.) You may choose not to respond to any question you feel uncomfortable answering.

1. On a scale of 1 to 10, please indicate how much pancreas pain you were having before your ESWL of the pancreas (please circle):
   1 2 3 4 5 6 7 8 9 10
2. On a scale of 1 to 10, please indicate how much pancreas pain you have currently (please circle):
   1 2 3 4 5 6 7 8 9 10
3. On a scale of 1 to 10, please indicate your overall quality of life with regard to your pancreas before your ESWL of the pancreas (please circle):
   1 2 3 4 5 6 7 8 9 10
4. On a scale of 1 to 10, please indicate your current quality of life with regard to your pancreas (please circle):
   1 2 3 4 5 6 7 8 9 10
5. Did you smoke tobacco at least once a week prior to having ESWL of your pancreas? (please circle)
   Yes No
6. Do you currently smoke tobacco at least once a week? (please circle)
   Yes No
7. If you are a prior smoker, what year did you quit smoking?
8. Did you require pain medications for your pancreas pain prior to undergoing ESWL of the pancreas? (please circle)
   Yes No

If yes, what medications did you require and how much of those medications did you require?

9. Do you currently require medications for your pancreas pain? (please circle)
   Yes No

If yes, what pain medications are you currently taking for your pancreas pain and how much of those medications do you currently require?

10. Did you drink at least one alcohol drink (beer, wine, or spirits) each day prior to having ESWL of your pancreas? (please circle)
    Yes No
11. Do you currently drink at least one alcohol drink (beer, wine, or spirits) each day on most days of the week? (please circle)
    Yes No
12. Did you have diabetes prior to undergoing ESWL of the pancreas? (please circle)
    Yes No
13. Do you currently have diabetes? (please circle)
    Yes No
14. Did you require pancreas enzyme replacement pills with meals prior to undergoing ESWL of the pancreas? (please circle)
    Yes No
15. Do you currently require pancreas enzyme replacement pills with meals? (please circle)
    Yes No
16. Since having ESWL of your pancreas, have you required surgery on your pancreas? (please circle)
    Yes No