

## ORIGINAL ARTICLE

# Endoscopic versus Surgical Drainage of the Pancreatic Duct in Chronic Pancreatitis

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## ABSTRACT

**BACKGROUND**

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For patients with chronic pancreatitis and a dilated pancreatic duct, ductal decompression is recommended. We conducted a randomized trial to compare endoscopic and surgical drainage of the pancreatic duct.

**METHODS**

All symptomatic patients with chronic pancreatitis and a distal obstruction of the pancreatic duct but without an inflammatory mass were eligible for the study. We randomly assigned patients to undergo endoscopic transampullary drainage of the pancreatic duct or operative pancreaticojejunostomy. The primary end point was the average Izbicki pain score during 2 years of follow-up. The secondary end points were pain relief at the end of follow-up, physical and mental health, morbidity, mortality, length of hospital stay, number of procedures undergone, and changes in pancreatic function.

**RESULTS**

Thirty-nine patients underwent randomization: 19 to endoscopic treatment (16 of whom underwent lithotripsy) and 20 to operative pancreaticojejunostomy. During the 24 months of follow-up, patients who underwent surgery, as compared with those who were treated endoscopically, had lower Izbicki pain scores (25 vs. 51,  $P<0.001$ ) and better physical health summary scores on the Medical Outcomes Study 36-Item Short-Form General Health Survey questionnaire ( $P=0.003$ ). At the end of follow-up, complete or partial pain relief was achieved in 32% of patients assigned to endoscopic drainage as compared with 75% of patients assigned to surgical drainage ( $P=0.007$ ). Rates of complications, length of hospital stay, and changes in pancreatic function were similar in the two treatment groups, but patients receiving endoscopic treatment required more procedures than did patients in the surgery group (a median of eight vs. three,  $P<0.001$ ).

**CONCLUSIONS**

Surgical drainage of the pancreatic duct was more effective than endoscopic treatment in patients with obstruction of the pancreatic duct due to chronic pancreatitis. (Current Controlled Trials number, ISRCTN04572410.)

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**I**N PATIENTS WITH CHRONIC PANCREATITIS, pain is the predominant symptom and remains a therapeutic challenge. Pancreatic-duct obstruction is considered an important etiologic factor; therefore, ductal decompression is advocated for patients with pain and a markedly dilated duct.

Both endoscopic and surgical drainage are treatment options. Surgical drainage is accomplished by longitudinal pancreaticojejunostomy<sup>1</sup> and has a rate of complications of 6 to 30%, a mortality rate of 0 to 2%, and a success rate in achieving long-term pain relief of 65 to 85%.<sup>2-9</sup> Endoscopic drainage involves sphincterotomy, dilation of strictures, and removal of stones and has a success rate of 30 to 100%.<sup>10-17</sup> We conducted a randomized trial to compare endoscopic and surgical drainage with respect to the outcomes of pain relief, physical and mental health, morbidity, mortality, length of hospital stay, number of procedures undergone, and changes in pancreatic function.

## METHODS

### PATIENTS

After approval of the study by the medical ethics committee of the Academic Medical Center (Amsterdam), patients were recruited from the Hepato-Pancreatico-Biliary outpatient clinic of this hospital, which functions as a tertiary referral center. All symptomatic patients were routinely evaluated by magnetic resonance cholangiopancreatography performed with a 1.5-tesla magnet (Siemens Vision) and contrast-enhanced computed tomography performed with a Philips MX8000 scanner. Written informed consent was obtained from all patients before enrollment (Table 1).

### ENDOSCOPIC DRAINAGE

Endoscopic treatment was performed by experienced endoscopists who had each performed more than 1000 endoscopic retrograde cholangiopancreatographic procedures. The procedure was performed with the patient under conscious sedation or, if endoscopy was preceded by shock-wave lithotripsy, with the patient under general anesthesia with propofol. A stenosis was considered to be present if the pancreatogram showed a narrowing of the main pancreatic duct, dilatation of the duct by more than 5 mm proximal to the narrowing, and incomplete distal runoff of the con-

**Table 1. Selection Criteria.**

#### Inclusion criteria

- Diagnosis of chronic pancreatitis, based on clinical symptoms and morphologic changes (e.g., calcifications and ductal changes) detected by imaging studies; pancreatic functional insufficiency; or both\*
- Obstruction of the pancreatic duct due to stenosis, intraductal stones, or both located left of the spine, with dilatation of the duct by at least 5 mm proximal to the obstruction, as determined by magnetic resonance cholangiopancreatography, abdominal computed tomography, or both
- Severe, recurrent pancreatic pain insufficiently relieved by non-narcotic analgesics or requiring opiates

#### Exclusion criteria

- Age <18 or >80 yr
- Enlargement of the pancreatic head >4 cm
- Contraindications to surgery
  - American Society of Anesthesiologists class IV†
  - Severe portal hypertension
- Contraindications to endoscopic treatment
  - Gastrectomy with Billroth II reconstruction
  - Other pancreatitis-related complications requiring surgery
- Previous pancreatic surgery
- Suspected pancreatic cancer
- Life expectancy <2 yr
- Pregnancy

\* Data are from Singer et al.<sup>18</sup> and Sarner and Cotton.<sup>19</sup>

† American Society of Anesthesiologists classification data are from Wolters et al.<sup>20</sup>

trast agent. After sphincterotomy, the decision to dilate the stricture, with either a balloon catheter or a Soehendra catheter, was made according to the judgment of the endoscopist. A 10-French Amsterdam biliary stent without side holes was inserted. If this was impossible, a 7- or 8.5-French stent was inserted and replaced by a 10-French stent within 6 weeks.

#### Intraductal Stones

If one or more intraductal stones more than 7 mm in diameter were identified by imaging studies, the patient was referred to Erasme Hospital, in Brussels, for lithotripsy.<sup>16,21</sup> The treatment was performed with the use of a lithotripter (Lithostar, Siemens) that provided shock waves of 0.28 to 0.54 mJ per square millimeter focused on the stones with a double x-ray system.<sup>22</sup> After lithotripsy, stone fragments were removed during a consecutive endoscopic transampullary drainage procedure with a balloon or Dormia basket and

the use of the “rotation–perfusion” technique.<sup>16</sup> If stone removal was incomplete, a 6-French nasopancreatic catheter was left in place, and lavage with saline (1 liter per 24 hours) was performed until the next round of treatment. If obstruction of the main duct could not be completely resolved, one or two endoprotheses were placed during the last endoscopic procedure.<sup>23</sup>

#### *Endoscopic Management during Follow-up*

All subsequent procedures took place in Amsterdam. If an endoprosthesis had been inserted, an elective endoscopic pancreatogram was scheduled for every 3 months. When complete runoff of contrast material was observed after removal of the stent and an extraction balloon could be passed through the pancreatic duct, endoscopic treatment was terminated. Persistent strictures were treated by repeated dilation and sequential insertion of multiple stents.

#### **SURGICAL DRAINAGE**

Surgery was performed within 4 weeks after randomization by experienced hepatobiliary surgeons. A pancreaticojejunostomy was performed by the method of Partington and Rochelle.<sup>1</sup> The pancreatic duct was incised over the full length up to 2 cm from the ampulla. When retrieval of concretions from the head area required further opening of the duct toward the ampulla, a limited wedge resection of pancreatic tissue was performed. The patency of the anastomosis was evaluated by means of magnetic resonance cholangiopancreatography 3 months after the procedure and again if symptoms recurred.

#### **COLLECTION OF BASELINE AND FOLLOW-UP DATA**

Information was obtained by the study coordinator during visits at baseline and at predefined intervals of 6 weeks, 3 months, 6 months, 12 months, 18 months, and 24 months after surgery or the first endoscopic procedure. Standardized evaluation of symptoms and laboratory investigations were performed. In addition, quality-of-life scores, as assessed by the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36) questionnaire,<sup>24</sup> and the Izbicki pain score<sup>25</sup> were obtained. The latter is a validated pain score, specifically designed for chronic pancreatitis, that is based on four questions regarding frequency of pain, intensity of pain (as indicated by a visual analogue score), use of analgesics, and disease-related

inability to work; the scale ranges from 0 to 100, with higher scores indicating more severe pain.

Data were collected regarding admission to the hospital and procedures performed. The procedures were classified as diagnostic or therapeutic. Therapeutic interventions encompassed all surgical and endoscopic procedures (including initial interventions), placement of jejunal feeding tubes, and endoscopic ultrasonography–guided nerve blockage. A lithotripsy session immediately followed by endoscopic drainage was considered a single intervention. Pancreatic endocrine function was evaluated by measuring fasting serum glucose levels and glycated hemoglobin levels and by collecting data on medication use. Pancreatic exocrine function was assessed by measuring fecal elastase levels.

#### **TREATMENT DURING FOLLOW-UP**

In patients with persistent or recurrent pain, imaging studies were repeated and evaluated by a multidisciplinary team of gastroenterologists, surgeons, and radiologists. If a recurrent pancreatic-duct obstruction was seen in a patient who had completed endoscopic treatment, stent therapy was resumed.

#### **OUTCOME MEASURES**

The primary outcome measure was pain during the 2-year follow-up period, expressed as the average of the Izbicki pain scores obtained at 6 weeks and at 3, 6, 12, 18, and 24 months. The secondary outcome measures were pain relief at the end of follow-up, physical and mental health, morbidity, mortality, length of hospital stay, number of procedures performed, and changes in exocrine and endocrine pancreatic function.

Pain relief at the end of follow-up was classified as complete (Izbicki pain score,  $\leq 10$ ) or partial (Izbicki pain score,  $>10$  after a decrease of  $>50\%$ ). Treatment was considered to have failed in patients whose treatment was converted from endoscopic drainage to surgery and in those who died because of treatment. Physical health and mental health were assessed according to the scores on the SF-36 questionnaire.<sup>24</sup>

Pancreatic function was expressed as the mean levels of fecal elastase, fasting serum glucose, and glycated hemoglobin at baseline and at the end of follow-up. Patients were considered to have endocrine insufficiency if they required treatment (either oral medication or insulin) for glycemic

control. During follow-up, treatment was initiated when the fasting glucose level was above 6.7 mmol per liter (121 mg per deciliter) and the glycated hemoglobin level was more than 6%. Exocrine insufficiency was defined as an elastase level of less than 200  $\mu$ g per gram of feces. The use of pancreatic enzymes was not considered to indicate pancreatic insufficiency, because they had also been prescribed as part of pain management. Changes in pancreatic function (both endocrine and exocrine) were evaluated by dividing the patients into four groups: those who had pancreatic insufficiency at both baseline and follow-up (insufficiency persisted), those who did not have insufficiency at baseline but in whom insufficiency developed during follow-up (insufficiency developed), those who had insufficiency at baseline but not at follow-up (insufficiency resolved), and those who did not have insufficiency at baseline or follow-up (sufficiency persisted).

#### STATISTICAL ANALYSIS

Randomization was performed with blocks of four or six patients by an automated assignment system that concealed the treatment assignments. No stratification was performed. Calculation of the sample size was based on the difference between the average Izbicki pain scores of the two treatment groups during follow-up. We determined that a study with 23 patients per group would have 90% power to detect a difference of 1 SD with the use of a two-group t-test at a two-sided significance level of 0.05. Hence, the sample size was set at 25 patients per group to allow for possible dropouts.

Depending on the distributional properties, outcome measures were expressed as means  $\pm$ SD or as medians with ranges. Analysis was performed according to the intention-to-treat principle. For each patient, the mean Izbicki pain score and the mean scores on the physical and mental health components of the SF-36 questionnaire were based on data obtained during follow-up. Missing follow-up data were considered to be missing at random. To adjust for baseline scores, analysis of covariance was performed.

Determination of pain relief and of changes in pancreatic function at the end of follow-up was based on the baseline data and the data from the last follow-up visit. Statistical significance was assessed with the use of Student's t-test for normally distributed continuous data (e.g., age); either

the chi-square test for categorical data (e.g., pain relief), with Yates' correction when appropriate (e.g., smoking), or Fisher's exact test for categorical data (e.g., changes in pancreatic function); and the Wilcoxon test for non-normally distributed continuous data (e.g., length of hospital stay). All reported P values are two-sided and were not adjusted for multiple testing.

A safety committee was appointed, which consisted of a gastroenterologist, a surgeon, and a radiologist who were not involved in the trial. The evolving trial results were known only to the primary investigator and were reported to this committee every 6 months. No formal rules for termination of the trial were defined in advance.

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## RESULTS

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#### ENROLLMENT AND TERMINATION OF THE TRIAL

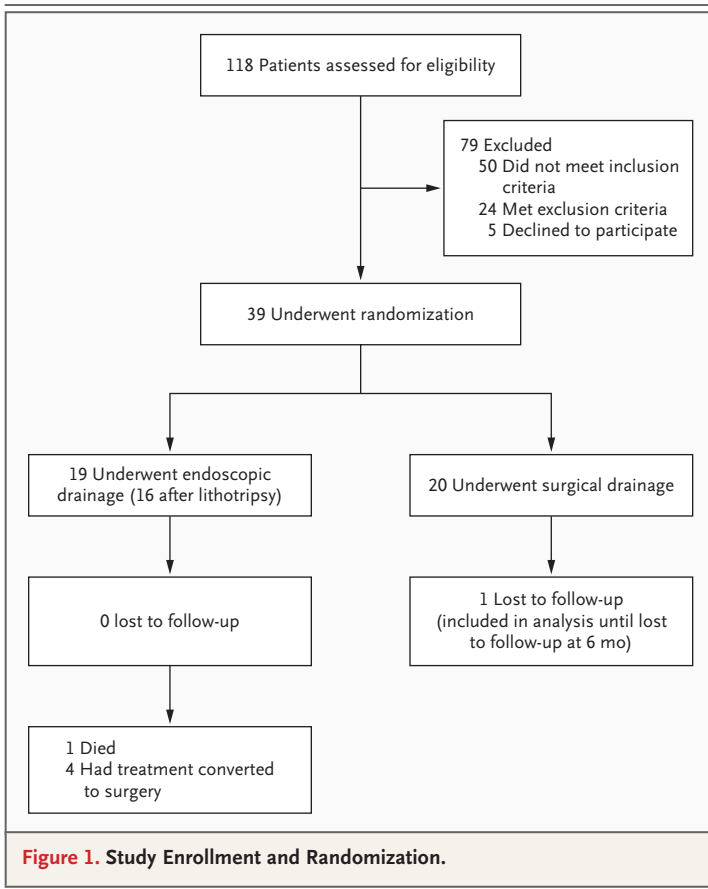
Between January 2000 and October 2004, a total of 118 patients were screened, and 39 underwent randomization (Fig. 1). After an unscheduled interim analysis, the study was terminated early by the safety committee on the basis of a significant difference in outcome ( $P < 0.001$ ) favoring the surgical group. At the date of termination, seven patients had not completed the follow-up period. The median follow-up time was 24 months (range, 6 to 24) for both groups. One patient was lost to follow-up 6 months after undergoing surgery. Available data from this patient were included in the analysis, but treatment of the patient with regard to pain relief was considered to have failed at the end of follow-up.

#### BASELINE CHARACTERISTICS OF THE PATIENTS

The demographic and clinical characteristics of the patients in the two treatment groups were similar, with the exception of ongoing alcohol abuse, which was present in five surgically treated patients and in none of the endoscopically treated patients (Table 2). Imaging studies of the pancreas performed before drainage showed intraductal concretions in 34 patients (87%), 27 of whom had multiple concretions. The mean diameter of the concretions was  $10 \pm 4$  mm.

#### ENDOSCOPIC TREATMENT

Nineteen patients were assigned to endoscopic treatment (Table 3) and underwent a median of 5 endoscopic procedures (range, 1 to 11). Pancreatic-duct obstruction was caused by a combina-



tion of strictures and stones in 15 patients (79%), by stones alone in 3 patients (16%), and by a stricture alone in 1 patient (5%).

Of the 18 patients with stones, complete stone extraction was accomplished in 16 (89%). Sixteen patients required lithotripsy. Eleven of the 16 patients had multiple stones; the median diameter of the largest stone was 11 mm (range, 6 to 20). Ten patients had a single lithotripsy session, and six patients required multiple sessions; the median number of sessions per patient was one (range, one to five).

One of the 19 patients died of a perforated duodenal ulcer 4 days after the last shock-wave lithotripsy session, resulting in a mortality rate of 5% for the endoscopic-treatment group. The patient was being treated with a nonsteroidal antiinflammatory drug, which may have had a role in the development and subsequent perforation of the ulcer. However, given the interval between treatment and death, a causative role of lithotripsy cannot be ruled out.

Sixteen patients (84%) had pancreatic-duct

strictures, all of which were distally located. Two patients had pancreas divisum with a stricture in the duct of Santorini. The stents were in place for a median of 27 weeks (range, 6 to 67). Balloon dilation was performed in 15 patients; 9 patients required sequential insertion of more than one stent, up to a maximum of three stents; and 7 patients had recurrent stenosis during follow-up for which stent therapy was resumed. Strictures were resolved in eight patients (50%).

The overall technical success rate of endoscopic treatment was 53%. The treatment of four patients was converted to surgery because of intractable pain, despite endoscopic treatment for persistent stenosis; only one had relief of pain after surgery. Three other patients had a stent at the time of data analysis (one at 2 years and two at 6 months after the initiation of endoscopic treatment). In addition, one patient with persistent stenosis remained asymptomatic and did not require further treatment.

After endoscopic treatment, 18 minor complications occurred in 11 of 19 patients (58%). In one patient, shock-wave lithotripsy caused a skin wound that persisted for 4 months. Five patients had stent-related complications, all of which were treated by replacement of the stent. Pancreatitis occurred in four patients, and cholecystitis in one; all these patients were treated conservatively.

#### SURGICAL TREATMENT

Of the 20 patients assigned to surgical treatment, 18 underwent a pancreaticojejunostomy (median length of the pancreatic-duct incision, 12 cm; range, 8 to 20). In one patient, a Whipple procedure was performed because of peripancreatic inflammation. In another patient, stone extraction required a Frey procedure.<sup>26</sup> All anastomoses remained patent during follow-up (technical success rate, 100%), as demonstrated by magnetic resonance cholangiopancreatography performed 3 months after surgery and during episodes of pain.

Seven patients (35%) had complications; no patients died. One patient required a repeated laparotomy because of leakage of the anastomosis. In two patients, bleeding from the operative site was suspected but not confirmed. Both patients were treated with blood transfusion. In addition, one patient had pneumonia, and three had wound infections.

## OUTCOMES

The primary and secondary outcomes are summarized in Table 3. The mean Izbicki pain score was  $51 \pm 23$  in the endoscopy group and  $25 \pm 15$  in the surgery group. After adjustment for baseline scores, the mean difference was 24 (95% confidence interval [CI], 11 to 36;  $P < 0.001$ ). Moreover, after surgical drainage, pain relief was immediate and was consistent during the follow-up period (Fig. 2). Complete or partial pain relief was achieved at the end of follow-up in 32% of patients in the endoscopy group and 75% of patients in the surgery group ( $P = 0.007$ ).

The follow-up scores on the physical health component of the SF-36 questionnaire were lower in endoscopically treated patients than in surgically treated patients, with a mean difference of  $-8$  (95% CI,  $-13$  to  $-3$ ;  $P = 0.003$ ) after adjustment for baseline scores. The two groups did not differ significantly with respect to length of hospital stay, but endoscopically treated patients underwent significantly more procedures than surgically treated patients (median, eight vs. three;  $P < 0.001$ ). More patients in the surgery group than in the endoscopy group had sufficient exocrine function at the end of the follow-up period, but the difference was not significant ( $P = 0.05$ ) (Table 3).

## DISCUSSION

Our study shows that in patients with chronic pancreatitis and pancreatic-duct obstruction, surgical drainage was more effective than endoscopic treatment during 2 years of follow-up. The benefits of surgery were demonstrated by more rapid, effective, and sustained pain relief. The surgical patients also had a better state of physical health and required fewer procedures. The difference in the mean Izbicki pain score between the treatment groups after adjustment for baseline differences was almost 24 points. The clinical relevance of this finding is substantial, since it reflects the difference between having no pain and having pain daily, or between taking no sick leave for pain and being permanently unable to work.

The observed outcome implies that surgical drainage leads to more effective decompression. One can hypothesize about explanations for this finding. First, during endoscopic treatment, outflow from secondary side branches might be compromised by the presence of a stent. In addition, after endoscopic treatment, recurrence of

**Table 2. Demographic and Clinical Characteristics of Patients at Randomization.\***

| Characteristic                  | Endoscopy (N=19) | Surgery (N=20) | P Value |
|---------------------------------|------------------|----------------|---------|
| Age — yr                        | 52±9             | 46±12          | 0.07    |
| Male sex — no. (%)              | 11 (58)          | 15 (75)        | 0.26    |
| Cause of pancreatitis — no. (%) |                  |                | 0.43    |
| Alcohol abuse                   | 9 (47)           | 12 (60)        |         |
| Idiopathic                      | 7 (37)           | 5 (25)         |         |
| Hereditary                      | 1 (5)            | 1 (5)          |         |
| Pancreas divisum                | 2 (11)           | 0              |         |
| Other                           | 0                | 2 (10)         |         |
| Pain pattern — no. (%)          |                  |                | 0.61    |
| Continuous                      | 12 (63)          | 11 (55)        |         |
| Intermittent                    | 7 (37)           | 9 (45)         |         |
| Izbicki pain score†             | 73±12            | 69±18          | 0.33    |
| Duration of symptoms — mo       | 16±14            | 21±19          | 0.45    |
| Ongoing alcohol abuse — no. (%) | 0                | 5 (25)         | 0.05    |
| Current smoker — no. (%)        | 15 (79)          | 17 (85)        | 0.94    |
| SF-36 quality-of-life scores‡   |                  |                |         |
| Physical health component       | 31±8             | 35±8           | 0.11    |
| Mental health component         | 33±8             | 37±12          | 0.43    |
| Exocrine function               |                  |                |         |
| Insufficiency — no. (%)§        | 13 (68)          | 16 (80)        | 0.65    |
| Fecal elastase — µg/g           | 125±125          | 139±145        |         |
| Endocrine function              |                  |                |         |
| Insufficiency — no. (%)¶        | 4 (21)           | 4 (20)         | 0.75    |
| Serum glucose — mmol/liter      | 6.5±2.5          | 6.1±2.7        |         |
| Glycated hemoglobin — %         | 6.3±1.2          | 6.2±1.3        |         |

\* Plus-minus values are means ±SD.

† The Izbicki pain score ranges from 0 to 100, with higher scores indicating more severe pain.

‡ Scores on the physical and mental health components of the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36) questionnaire range from 0 to 100, with higher scores indicating better quality of life. Linear transformations were performed to standardize the scores to a mean score of  $50 \pm 10$  in a general Dutch population.

§ Exocrine insufficiency was defined as an elastase level of less than 200 µg per gram of feces.

¶ Endocrine insufficiency was defined as the need for treatment for glycemic control (either oral medication or insulin). Treatment was initiated during follow-up in patients who had fasting glucose levels of more than 6.7 mmol per liter (120 mg per deciliter) in combination with a level of glycated hemoglobin of more than 6%.

|| To convert values for glucose to milligrams per deciliter, divide by 0.056.

strictures and formation of new intraductal stones are common, as we observed in this cohort of patients. Endoscopic stenting might even facilitate these conditions, since it has been shown to worsen pancreatic-duct abnormalities.<sup>27</sup> An advantage of surgery might be that the longitudi-

**Table 3. Outcomes of Endoscopic and Surgical Treatment after 2 Years of Follow-up.\***

| Variable   | Endoscopy<br>(N=19) | Surgery<br>(N=20) | Endoscopic Results vs. Surgical<br>Results (95% CI) | P Value |
|--|---------------------|-------------------|---|---------|
| Izbicki pain score†                                    | 51±23               | 25±15             | 24 (11 to 36)‡                                      | <0.001  |
| Pain relief — no. (%)§                                 | 6 (32)              | 15 (75)           | -43 (-72 to -15)¶                                   | 0.007   |
| Complete relief  | 3 (16)              | 8 (40)            |   |         |
| Partial relief   | 3 (16)              | 7 (35)            |   |         |
| No relief  | 13 (68)             | 5 (25)            |   |         |
| Conversion to surgery — no. (%)                        | 4 (21)              | NA                |   |         |
| Technical success — no. (%)                            | 10 (53)             | 20 (100)          | -47 (-70 to -25)¶                                   | <0.001  |
| Complications — no. (%)                                | 11 (58)             | 7 (35)            | 23 (-8 to 53)¶                                      | 0.15    |
| Major  | 0                   | 1 (5)             |   |         |
| Minor  | 11 (58)             | 6 (30)            |   |         |
| Death — no. (%)  | 1 (5)               | 0                 | 5 (-5 to 15)¶                                       | 0.49    |
| Hospital stay — median no. of days (range)             | 8 (0–128)           | 11 (5–59)         | -3 (-9 to 4)¶                                       | 0.13    |
| Hospital readmittance — median no. of patients (range) | 1 (0–5)             | 0 (0–7)           |   |         |
| Procedures — median no. (range)                        | 8 (1–21)            | 3 (1–9)           | 5 (2 to 8)¶   | <0.001  |
| Diagnostic   | 3 (0–11)            | 2 (0–8)           |   |         |
| Therapeutic**  | 5 (1–11)            | 1 (1–5)           |   |         |
| SF-36 quality-of-life scores††                         |                     |                   |   |         |
| Physical health component                              | 38±9                | 47±7              | -8 (-13 to -3)‡                                     | 0.003   |
| Mental health component                                | 40±9                | 45±9              | -3 (-8 to 1)‡                                       | 0.15    |
| Exocrine function                                      |                     |                   |   | 0.05    |
| Insufficiency persisted — no. (%)                      | 11 (61)             | 13 (65)           |   |         |
| Insufficiency developed — no. (%)                      | 6 (33)              | 1 (5)             |   |         |
| Insufficiency resolved — no. (%)                       | 1 (6)               | 3 (15)            |   |         |
| Sufficiency persisted — no. (%)                        | 0                   | 3 (15)            |   |         |
| Fecal elastase — µg/g                                  | 56±74               | 145±189           |   |         |
| Endocrine function                                     |                     |                   |   | 0.48    |
| Insufficiency persisted — no. (%)                      | 3 (17)              | 4 (20)            |   |         |
| Insufficiency developed — no. (%)                      | 3 (17)              | 1 (5)             |   |         |
| Insufficiency resolved — no. (%)                       | 1 (6)               | 0                 |   |         |
| Sufficiency persisted — no. (%)                        | 11 (60)             | 15 (75)           |   |         |
| Serum glucose — mmol/liter‡‡                           | 6.8±3.2             | 5.9±1.6           |   |         |
| Glycated hemoglobin — %                                | 6.4±1.2             | 6.2±1.3           |   |         |

\* Follow-up data were available for all patients except for one deceased patient in the endoscopy group. Treatment of the deceased patient was considered to have failed with respect to pain relief. Follow-up data regarding the Izbicki pain scores and scores on the physical and mental health components of the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36) questionnaire were available for 96.9% and 93.1% of all possible measurements in the endoscopy and surgery groups, respectively. These percentages were determined with the exclusion of measurements censored because of death (6 scores) and the early stopping of the trial (15 scores for eight patients). Individual mean scores based on available follow-up data were calculated for all surviving patients. Missing data were considered to be missing at random. Five of 18 end-of-follow-up measurements of elastase, glucose, or glycated hemoglobin in the endoscopy group were based on a follow-up period of less than 2 years. Four of 20 end-of-follow-up measurements of elastase and 2 of 20 measurements of glucose or glycated hemoglobin in the surgery group were based on a follow-up period of less than 2 years. Plus–minus values are means ±SD. CI denotes confidence interval, and NA not applicable.

† The Izbicki pain score ranges from 0 to 100, with higher scores indicating more severe pain.

‡ The mean difference between groups was calculated after analysis of covariance with adjustment for baseline scores.

§ Pain relief at the end of follow-up was classified as complete (Izbicki pain score, ≤10) or partial (Izbicki pain score, >10 after a decrease of >50%).

¶ This is the absolute difference between the percentages.

|| This is the difference between the medians.

\*\* Therapeutic interventions encompassed all surgical and endoscopic procedures (including initial interventions), placement of jejunal feeding tubes, and endoscopic ultrasonography–guided nerve blockage.

†† The scores on the SF-36 physical and mental health components range from 0 to 100, with higher scores indicating better quality of life. Linear transformations were performed to standardize the scores to a mean score of 50±10 in a general Dutch population.

‡‡ To convert values for glucose to milligrams per deciliter, divide by 0.056.

nal anastomosis ensures drainage over the full length of the pancreas. Furthermore, opening of the pancreatic capsule during surgical drainage might alleviate interstitial pressure.<sup>28</sup>

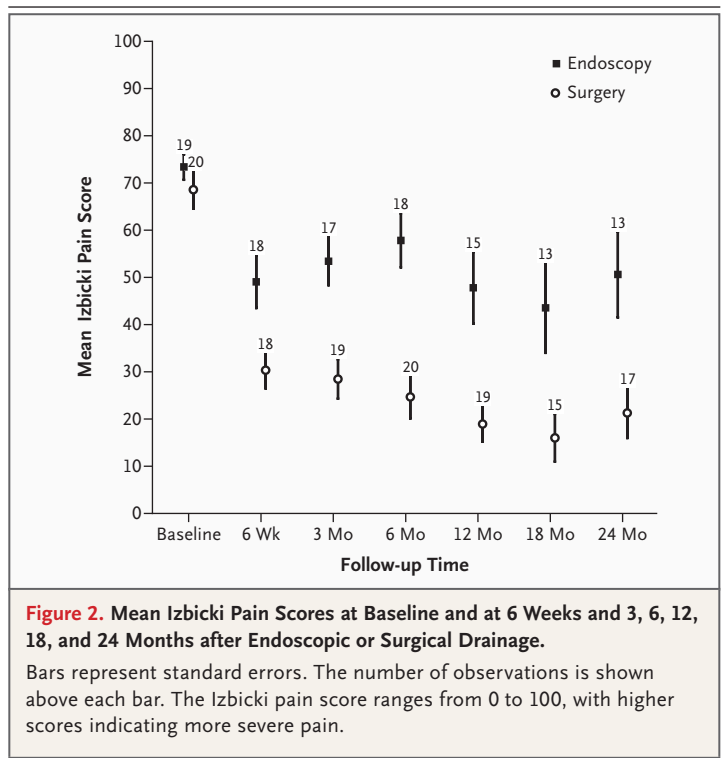
Over the years, a number of retrospective studies have evaluated endoscopic treatment of pancreatitis,<sup>10-13,15-17,29,30</sup> and all have reported pain reduction in the majority of patients. However, these studies had similar flaws in design: they were noncomparative, used treatment protocols that were not well defined, and most important, failed to use a validated measure to assess pain.

Eleftheriadis recently reported the results of a retrospective analysis of patients with chronic pancreatitis who underwent endoscopic treatment in the center where our study population had shock-wave lithotripsy.<sup>31</sup> The long-term response rate was 62%, which is higher than that in the present study. The major difference between our study protocol and that of Eleftheriadis is that in the latter, stent exchanges were performed “on demand,” when a patient indicated that he or she was in pain. As a result, the median duration of stenting in that study (23 months) was much longer than in our study (27 weeks).

It has been suggested that the effects of endoscopic treatment may occur only after months or even years of treatment, but this remains to be proved.<sup>12,32</sup> In the present study, stent therapy was resumed in patients who had a symptomatic recurrent obstruction. The shorter duration of stenting alone, therefore, does not account for the observed difference in outcomes. In addition, because many patients had substantial pain during endoscopic treatment, the rationality of using stent therapy is questionable.

We are aware of only one other published prospective, randomized trial comparing endoscopic treatment with surgery.<sup>33</sup> The results are in agreement with our findings, with a reported benefit of surgical treatment (complete pain relief in 37% of patients undergoing surgery vs. 14% of those receiving endoscopic treatment). However, the design of that study makes the interpretation of results difficult. Because treatment was tailored to the patient, surgery involved resection in the majority of patients. Furthermore, endoscopic-drainage techniques were not optimally applied, in that they did not include shock-wave lithotripsy, cumulative stenting, or repeated treatment after recurrence of symptoms.

In the present study, pain was assessed by



means of a validated scoring system specifically designed for chronic pancreatitis. Furthermore, in contrast to previous studies, clinical success in terms of pain relief was strictly defined. Nevertheless, the subjectivity of pain assessment and the unblinded study design might have biased the results. To minimize expectation bias, patients completed the questionnaires in private, and only the study coordinator had access to clinical reports.

Another feature of our study is that the patients were treated in centers with experts in endoscopic treatment of pancreatitis and shock-wave lithotripsy. These are demanding procedures, and the results may be worse in less experienced hands. In contrast, pancreaticojejunostomy is considered a relatively easy procedure to perform. In the future, this operation might be performed laparoscopically, making it even less invasive.<sup>34</sup>

The results of the present study cannot be extrapolated to all patients with ductal obstruction due to chronic pancreatitis. We explicitly excluded patients with an inflammatory mass, because treatment of this condition requires a combination of ductal drainage and a limited resection of the pancreatic head by the Beger or the Frey procedure.<sup>35,36</sup> Furthermore, our cohort had complex pathologic features, with a combination of stric-

ture and stones in most patients. On the basis of the outcome of the study, we regard surgical drainage as the preferred treatment in such patients. In cases of less extensive disease, endoscopic treatment may still be a valuable alternative, and future studies should be aimed at answering this question.

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