

Natural course of operated pseudocysts in chronic pancreatitis

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Abstract

A longterm review (median follow up 11 years) of the postoperative course of pancreatic pseudocysts was undertaken in 55 patients with chronic pancreatitis. While 96% of the patients were free of pain immediately after the operation this figure fell to 53% subsequently. Alcohol abstinence did not significantly reduce pain. Endocrine pancreatic deterioration (60%) was significantly ($p=0.0059$) more frequent than exocrine (38%). Unemployment increased from 2 to 41%; retirement rose from 0 to 33%, mainly as a result of pancreatitis. Twenty one (38%) patients died. Chronic pancreatitis related death rate was 14%. Three patients died of extrapancreatic carcinomas.

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Every third to fourth patient with chronic pancreatitis develops pancreatic pseudocysts,^{1,2} which account for abdominal pain³ and for about two thirds of all operations in chronic pancreatitis patients.² In contrast with the well reported course of pancreatic pseudocysts in acute pancreatitis,⁴ data on chronic pancreatitis are lacking.

Generally, drainage and resective operations in chronic pancreatitis cases bring immediate pain relief for 80-90% of the patients.⁵ Whether operative treatment is successful in the long run will depend on follow up results at 2.5 and 10 year intervals.⁶

This study aims at evaluating the longterm postoperative course of chronic pancreatitis in patients operated on for pancreatic pseudocysts, with special attention to pain, exocrine, and endocrine pancreatic function and prognosis of the disease.

Patients and methods

This study includes 55 chronic pancreatitis patients (43 males, 12 females; mean age 40 years, range 21 to 64), who were operated on for pancreatic pseudocysts. Diagnosis of chronic pancreatitis was based on clinical evaluation, at least one abnormal secretin-pancreozymin test^{7,8} performed more than three months after the last pain episode, plain abdominal x ray ($n=53$), and faecal fat estimation ($n=55$).⁹

Cause of pancreatitis was alcoholism in 45 (82%) patients, idiopathic in nine (16%), and familial in the remaining patients (2%). Pancreatic calcifications showed up on plain abdominal x ray in 37 (70%) patients.

Single or multiple pancreatic pseudocysts were diagnosed by ultrasound in 32 patients and before ultrasound was introduced into the diagnostic procedures in the remaining 23 patients by hypotonic duodenography or other x ray studies, or both, later confirmed by operation. Forty four (80%) patients had one, nine (16%), two, and two (4%) patients, three pseudocysts. In 42 (76%) of the patients, a cystojejunostomy was performed, in seven (13%), a Whipple's operation, and in six (11%), a left sided resection.

The duration of the disease was defined as the time from the onset of symptoms or the first stay in hospital, or both, until the end of the observation period. Postoperative mean (SD) observation time was 12.4 (8.3) years (median 11.0 years).

'Free from pain' ('pain relief') meant without episodes of pain for more than one year.

Severity of pancreatic insufficiency was graded on the basis of a secretin-pancreozymin test and faecal fat analysis as follows: absent=normal; slight=reduced enzyme output; moderate=reduced bicarbonate concentration and enzyme output, faecal fat still normal; severe=abnormal secretin-pancreozymin test and steatorrhoea.⁷

Diabetes mellitus, in line with the World Health Organisation definition, meant endocrine pancreatic insufficiency. It was classified according to treatment as follows: absent=normal fasted blood glucose or normal glucose tolerance test, or both; moderate=diet alone or diet plus oral drugs; severe=diet plus insulin.

Information concerning recurrence of pain and other follow up parameters was gathered during examination in the hospital or by questionnaires sent to the patients, or both.

Follow up examination of exocrine and endocrine pancreatic function consisted of a secretin-pancreozymin test (when possible) plus faecal fat estimation and an oral glucose tolerance test or blood glucose profiles.

For statistical analysis, the Fisher's exact test (Table I) and a χ^2 test of independence (Table II and comparative data on postoperative pain overleaf) were used.

Results

PAIN

Pain relief (without pain >1 year) occurred postoperatively in 53 (96%) patients. It occurred immediately after operation in 37 patients, whereas 16 patients did not report clearly enough to determine the exact postoperative time of pain relief. Only two (4%) patients complained of persisting severe pain.

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TABLE I Pain relief and drinking habits by the end of the observation time in 45 patients with alcohol induced chronic pancreatitis operated for pancreatic pseudocysts

Drinking habits	Number	Pain relief	
		(n)	(%)
Continued to drink	28	13	46
Stopped drinking	17	12	71
Total	45	25	56

By the end of observation time, however, only 29 (53%) patients were free of pain, 26 (47%) not. Those who were pain free consisted of 23, two, and four patients who had undergone drainage operation and a Whipple's or left sided resection respectively and those with pain consisted of 19, five, and two patients who had undergone the same respective operations. Pain relief was independent of the surgical procedure (drainage or resection, $p=0.59$; drainage, Whipple's operation, left sided resection, $p=0.34$).

Seventeen of 45 patients with alcohol induced chronic pancreatitis stopped drinking. Pain relief was much more frequent in abstainers than in non-abstainers (71% *v* 46%), although the effect of abstinence because of the small number of patients was not significant (Table I, $p=0.3$).

EXOCRINE PANCREATIC INSUFFICIENCY

At the time of diagnosis, exocrine pancreatic insufficiency was slight in 12 (22%), moderate in 17 (31%), and severe in 24 (44%) patients. In two (4%) patients, a normal secretin-pancreozymin test at the initial investigation turned abnormal before operation.

An evaluation of postoperative exocrine pancreatic insufficiency by means of a secretin-pancreozymin test and faecal fat estimation was possible for anatomical reasons in only 34 patients.

An improvement was found in five (15%) patients either from severe to moderate ($n=3$) or from moderate to slight exocrine pancreatic insufficiency ($n=2$). In 16 (47%) patients, the test results remained unchanged, and in 13 (38%) patients, they had not deteriorated (Table II).

At the end of observation period, 15 (27%) patients had slight, 17 (31%) moderate, and 23 (42%) severe exocrine pancreatic insufficiency.

TABLE II Course of exocrine and endocrine pancreatic insufficiency in patients with chronic pancreatitis operated for pancreatic pseudocysts

Course	Exocrine pancreatic insufficiency ($n=34$)*		Endocrine pancreatic insufficiency ($n=55$)	
	(n)	(%)	(n)	(%)
Improvement	5	15	0	0
No change	16	47	22	40
Deterioration	13	38	33	60†

*In 21 patients, a secretin-pancreozymin test was postoperatively not possible because of anatomical reasons.
† $p=0.0059$.

ENDOCRINE PANCREATIC INSUFFICIENCY

Normal endocrine pancreatic function was initially diagnosed in 30 (55%) patients, moderate insufficiency in 25 (46%). No patient had required insulin before the operation.

During the longterm follow up (median 11 years), there was no improvement of endocrine pancreatic function in any cases, but deterioration in 33 (60%) patients, being significantly more frequent ($p=0.0059$) than in exocrine pancreatic insufficiency. No change in endocrine test results was seen in 22 (40%) patients (Table II).

At the end of the observation period, nine (17%) patients still had a normal endocrine pancreatic function, whereas 15 (27%) had moderate, and 31 (56%) severe, insulin requiring endocrine pancreatic insufficiency.

SOCIOECONOMIC STATUS

At the beginning of the observation period, with one exception, all patients were either employed or worked in the home. By the end of the observation period, only 32 (59%) of 54 patients were still capable of working; four patients were unemployed, and 18 (33%) patients had retired. Retirement was due to pancreatitis in 10 (56%) of these patients. From one patient, no clear information was obtained about his working ability.

MORTALITY

Within the observation period, more than one third of the patients died (21 (38%) patients). The cause of death was unknown in six patients, caused by pancreatitis in three, and in the remaining 12 patients unrelated to the underlying disease. There were no cases of pancreatic carcinoma, but three patients died of an extrapancreatic carcinoma (brain tumour, oral cavity carcinoma, rectum carcinoma).

Discussion

PAIN

The Zurich group and others have concluded that pain decreases with the progression of the underlying disease,¹⁰⁻¹² because 84% of their patients with calcifying alcoholic pancreatitis experienced lasting pain relief within a median of 4.5 years from onset. In a similar study of 335 patients (27% of whom had surgery), we found that even after a follow up of more than 10 years, only 46.7% of the patients became pain free.¹³ As a continuation of this study, we report now on a subgroup of patients with operated pancreatic pseudocysts. With two exceptions, all were free of pain immediately after operation, but only 53% stayed pain free during follow up. One flaw of this retrospective study is that it does not include a pain score for the severity of pain. Pain episodes were only reported, however, if the patient had either consulted a doctor or the clinic and received pain killing treatment.

The recurrence of pain in the other 26 (47%) patients was independent of the surgical procedure and may reflect the progression of the disease, or the continuation of alcohol abuse as the underlying aetiological factor, or both. In the only other longterm follow up study on the course of operated pancreatic pseudocysts, pain relief was considered to be poor in 18 (43%) of 42 patients after 13 years, but this series mixed patients with acute and chronic pancreatitis.¹⁴

ALCOHOL INTAKE

We have previously reported that the incidence of pain relief among abstainers was higher than among non-abstainers, but not significant.¹³ This is essentially in agreement with two other studies.^{15 16} In contrast, previous studies^{12 17} had suggested that pain decreases with the duration of alcoholic pancreatitis as long as the patient refrains from alcohol.

In this study, the noticeable beneficial influence of alcohol abstinence on pain agrees with two other studies on postoperative pain and prognosis for pancreatic pseudocysts in general.^{14 18}

EXOCRINE PANCREATIC INSUFFICIENCY

Three previous studies^{13 19 20} on the natural course of chronic pancreatitis have questioned the inference that chronic pancreatitis leads, in the long run, to progressively deteriorating exocrine pancreatic function. We have found previously an improvement in 11.2% and no change in 46.2%.¹³ The improvement we found agrees with three reports,²¹⁻²³ but differs from one report¹² in which severely deteriorating exocrine pancreatic insufficiency was established by faecal chymotrypsin.

Similar improvement percentages were also found in our subgroup of patients with pancreatic pseudocysts, which is in agreement with a prospective study by Nealon and Thompson.²⁴ They reported that pancreaticojejunostomy in patients with large ducts and in whom severe morphological changes and exocrine and endocrine pancreatic insufficiency had not occurred early, retarded further progression of exocrine and endocrine insufficiency, regardless of whether the patients abstained from alcohol or not.

ENDOCRINE PANCREATIC INSUFFICIENCY

Endocrine pancreatic insufficiency in patients with chronic pancreatitis either deteriorates or remains unchanged, but shows no improvement.^{12 13 19 23 25 26} This was also shown in our patients with operated pancreatic pseudocysts.

SOCIOECONOMIC SITUATION

Data on the implications of chronic pancreatitis for the socioeconomic status of patients is not forthcoming in most studies on chronic pancreatitis. Despite the sharp increase in retirement and unemployment among patients in our previous study¹³ and in

the subgroup of patients with pancreatic pseudocysts, the drop in social status was not as significant as in the study of Thorsgaard Pedersen *et al.*¹⁹

MORTALITY

It is difficult to compare data on mortality because the studies vary considerably in the length of observation time. In our previous evaluation of the natural course of chronic pancreatitis, we found a death rate of 21.8% during a mean SD follow up of 11.3 (8.3) years (median 9.8).¹³ The two other studies, comparable with ours,^{12 23} showed similar data. The distinctly higher death rate in the subgroup of patients with pancreatic pseudocysts of over one third possibly reflects either the severity of this complication of the disease or the longer observation period.

The incidence of patients with pancreatic and extrapancreatic carcinoma in chronic pancreatitis is still a matter of debate.^{12 13 15 23 27-29} The number of patients with pancreatic pseudocysts in our study is too small for further conclusions. But the incidence of extrapancreatic carcinoma should remind the clinician to be aware of this possibility in chronic pancreatitis complicated by pancreatic pseudocysts.

It is hoped that our study will stimulate a new direction for future investigations of pancreatic pseudocysts. For example: (1) When such factors as alcohol abstinence and time do not make a significant difference in pain relief, what other factors could be important? (2) What factors correlate with exocrine pancreatic insufficiency improvement and standstill in endocrine pancreatic insufficiency? (3) What stress factors in the socioeconomic status of patients could influence prognosis?

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