The Inflammatory Pancreatic Head Mass

Significant Differences in the Anatomic Pathology of German and American Patients With Chronic Pancreatitis Determine Very Different Surgical Strategies

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Background: The indications for surgery and the surgical strategy selected for chronic pancreatitis (CP) vary widely, perhaps because of unaccounted characteristics of different patient populations such as the "inflammatory mass" in the head of the pancreas, commonly described in Europe but not in America.

Methods: We compared the pancreatic morphology, anatomic complications, indications leading to intervention, and the operation performed in 93 consecutive patients with CP operated upon either at a German (n = 48) or an American (n = 45) center specializing in pancreatic surgery. Pretreatment computed tomography/magnetic resonance imaging scans were reevaluated by 2 independent radiologists, especially to measure the anterior-posterior diameter of the pancreatic head (the inflammatory mass).

Results: The prevalence of endocrine and exocrine insufficiency was not significantly different. The median diameter of the pancreatic head mass was significantly larger in the German group (4.5 cm, P < 0.001). Inflammatory mass-dependent symptoms [gastric outlet obstruction (9/48 vs. 1/45; P = 0.02) and hemorrhage (7/48 vs. 0/45; P = 0.015)] were more frequent in the German group. Bile duct stenosis (19/48 vs. 11/43; P = 0.18) and suspicion of malignancy (5/48 vs. 11/43; P = 0.10) were comparable, whereas chronic pain (15/48 vs. 28/43; P = 0.001) was a more frequent indication for surgery in the US group. Splenic or portal vein thrombosis was found only in the German group. The duration of nonoperative therapy was significantly longer in the German group (median 56 vs. 26 months; P = 0.02). In the US group, a pancreatoduodenectomy with antrectomy was performed in most (89%) cases, whereas in the German group a duodenum-preserving head resection was preferred in more than half (25/47) of the cases (P < 0.001).

Conclusions: Symptoms, duration of conservative therapy, and selection of surgical treatment all differed significantly between German and American patients with CP. These differences seem to be dependent upon surprising but unexplained disparities in the pathologic pancreatic anatomy between the 2 populations.


In the Western world the incidence of chronic pancreatitis (CP) is currently 5 to 10 newly diagnosed patients per 100,000.1,2 In Asia, the incidence seems to be even higher.3 The principal symptom manifestations of CP are chronic or recurrent pain, and, in later stages, exocrine and endocrine insufficiency.4 Also, in advanced stages of CP, the development of anatomic complications that may require intervention include biliary obstruction, gastric outlet obstruction, pseudocysts, hemorrhage from pseudoaneurysms into pseudocysts or into the gastrointestinal tract, pancreatic fistulas, and stenosis or occlusion of the portal venous system.5–8

The indications and the appropriate time for surgical intervention have not reached consensus among gastroenterologists and surgeons8,9,10 because of competing technologies, lack of standard criteria, and a paucity of valid clinical trials. The goal of spontaneous resolution of pain by progressive burn-out of the gland is still pursued by some physicians, but this strategy leaves the patient symptomatic for an indefinite number of years, dependent on narcotic medication and still facing the risk of failure of this approach.5,11 Diverse guidelines for therapy for CP, often reflecting parochial national viewpoints, have been proposed through consensus conferences10,12–16 but without agreement. Withholding potential beneficial surgical treatment may not only prolong remediable suffering,17 but also allow development of further complications like portal vein thrombosis, which may make operative therapy hazardous or even impossible due to increased intraoperative bleeding.5,8,18

The inflammatory process in the pancreatic head has been blamed as the pacemaker of both pain and progression of the disease, perhaps mediated through pancreatic duct obstruction, parenchymal hypertension, or sensory nerve injury.9,10 Surgical strategy in CP has thus been directed at the pancreatic head with a variety of tactics including pancreatoduodenectomy (Whipple procedure with or without pylorus preservation) and partial resection of the pancreatic head with pancreatic duct drainage (Frey operation,19 Beger procedure20). In part, the selection of operation, especially the partial head resections, is based on the concept of an inflammatory mass (“tumor”) involving the pancreatic head. The description of this inflammatory tumor has been noted and accepted primarily in European centers.21,22 It is not clear that the phenomenon of the pancreatic head mass has been similarly recognized in US centers.

This study was initiated to compare and contrast the presentation, classification, and management of patients with CP chosen for potential surgical therapy in a German and an American center. For this purpose, we enrolled and evaluated 93 consecutive patients treated in the departments of surgery either at the Albert-Ludwigs-University Hospital in Freiburg, Germany, or the Massachusetts General Hospital, Boston.

PATIENTS AND METHODS

The data of 93 consecutive patients with CP at the 2 departments of surgery were analyzed. In the German center, the time of first presentation of the 48 patients was between 2001 and 2005; in the US center, the 45 patients initially were seen first between 1995

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and 2005. The few patients (3 in Boston, none in Freiburg) whose predominant lesion was only a very dilated pancreatic duct and who were thus selected for lateral pancreaticojejunostomy (Puestow procedure) were excluded from this analysis.

The details obtained from the prospective databases at the 2 institutions included demographic data, symptoms, radiologic findings, and laboratory values. The presence of biliary stenosis, duodenal stenosis, pseudocysts, and involvement of the portal venous system or visceral arteries was documented. The leading indication for surgical treatment and the operation chosen were registered. Two radiologists independently and without knowledge of the surgical intervention reanalyzed the preoperative radiographic studies for maximum diameter of the pancreatic head, stenosis/thrombosis of the superior mesenteric, splenic and portal vein, and biliary or duodenal stenosis. The diagnosis of CP was (postoperatively) histologically proven in 36 patients (75%) in the German group and in 43 patients (96%) in the US group. The remaining 14 patients, who did not have fibrotic changes sufficient for unequivocal tissue diagnosis, all had characteristic morphologic signs of CP in cross-sectional imaging, severe upper abdominal pain with radiation to the back, or pancreatic exocrine/endocrine insufficiency.

Surgeons from each institution spent time on site at the other center to review the data independently and to produce a validated consensus. All 45 patients of the US group had an operative procedure. Forty-two of 48 Germans had an operation; of the other 6, 3 had a CT-guided drainage of infected pseudocysts, and 1 patient was not a candidate for surgery because of excessive comorbidity. Two patients in the German group refused the proposed surgical treatment.

Statistics

All data were recorded and statistically analyzed with SPSS 14.0 for Windows (SPSS, Chicago, IL). Differences between the German and American groups were compared by χ² test, Wilcoxon test, and Fisher exact test where applicable.

RESULTS

Clinical Characteristics

Except for a slightly higher proportion of women among the American patients, the clinical characteristics of the 2 groups were similar (Table 1).

Morphologic Characteristics of the Pancreas and Their Consequences

As demonstrated by cross-sectional imaging, the median anterior-posterior diameter of the pancreatic head was significantly larger in the German group than in the American patients [4.5 cm (2.8–10) vs. 2.6 cm (0.8–5.8), P = 0.001] (Fig. 1) (Table 2). This difference explains the greater use of the description “pancreatic head mass” in Germany. Figure 2 shows representative CT scans of the predominant German and American anatomic characteristics of the pancreatic head in CP. In 6 cases, there was an extensive lymphoplasmacytic infiltrate in the pancreatic head in the Freiburg patients, but no instances in the Boston specimens.

Bile Duct and Duodenal Involvement

Median preoperative bilirubin and alkaline phosphatase levels were significantly higher in the German group: at least 1 of those 2 parameters indicating cholestasis was greater than normal in 46% of the cases versus only 4% in the US group (P < 0.001) (Table 2). By cross-sectional imaging, however, there was proximal dilation of the common bile duct in 40% of the Germans and in 26% of the Americans (P = ns). Clinically relevant duodenal stenosis was documented in 9 patients in the German group but in only 1 patient in the US group (P < 0.02).

Major Vascular Complications

Hemorrhage into the gastrointestinal tract from pseudoaneurysms occurred significantly more frequently in the German patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Germany</th>
<th>United States</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients n = 48</td>
<td>n = 45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (f/m)</td>
<td>11/37</td>
<td>20/25</td>
<td>0.05</td>
</tr>
<tr>
<td>Age (yr, median, range)</td>
<td>49 (35–64)</td>
<td>52 (13–79)</td>
<td>0.09</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18%</td>
<td>20%</td>
<td>1.00</td>
</tr>
<tr>
<td>Exocrine insufficiency</td>
<td>40%</td>
<td>29%</td>
<td>0.27</td>
</tr>
<tr>
<td>Cholangitis</td>
<td>17%</td>
<td>4%</td>
<td>0.09</td>
</tr>
<tr>
<td>Recurrent acute pancreatitis</td>
<td>38%</td>
<td>57%</td>
<td>0.10</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>66%</td>
<td>71%</td>
<td>0.65</td>
</tr>
</tbody>
</table>
TABLE 2. Anatomical Characteristics and Complications of Chronic Pancreatitis in the German (n = 48) and American (n = 45) Group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Germany</th>
<th>United States</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP diameter of the pancreatic head (cm) median (range)</td>
<td>4.5 (2.8–10) cm</td>
<td>2.6 (0.5–8) cm</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alkaline phosphatase Median (range)</td>
<td>227 (0–260) U/L</td>
<td>110 (3–304) U/L</td>
<td>0.01</td>
</tr>
<tr>
<td>Bilirubin Median (range)</td>
<td>1.5 (0.1–24) mg/dL</td>
<td>0.46 (0.2–1.5) mg/dL</td>
<td>0.001</td>
</tr>
<tr>
<td>Chemical cholestasis*</td>
<td>46%</td>
<td>4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CBD stenosis†</td>
<td>19 (40%)</td>
<td>11 (26%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Duodenal stenosis</td>
<td>9 (19%)</td>
<td>1 (2%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Pancreato-pleural fistula</td>
<td>3 (6%)</td>
<td>0%</td>
<td>0.02</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>7 (15%)</td>
<td>0%</td>
<td>0.01</td>
</tr>
<tr>
<td>Occlusion splenic vein</td>
<td>14 (29%)</td>
<td>0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PV/SMV stenosis or thrombosis</td>
<td>8 (15%)</td>
<td>(1) 2%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Preoperative data were unavailable in the US group regarding CBD-stenosis in 2 patients.
*Bilirubin and/or alkaline phosphatase elevated.
†Radiologically demonstrated prestenotic CBD-dilation.
CBD indicates common bile duct; SMV, superior mesenteric vein; PV, portal vein; SD, standard deviation.

Chronic pain was the most frequent symptom in both groups, but in the US population it was much more often the main indication for surgical therapy (15/48 (Germany) vs. 28/45 (United States); P = 0.001). In contrast, gastric outlet/duodenal obstruction was significantly more frequent in the German group (8/47 vs. 1/45; P = 0.03) and severe complications leading to urgent surgical interventions [hemorrhage (7/48 vs. 0/45; P = 0.013), pancreato-pleural fistulas/infected pseudocysts (10/48 vs. 0/45; P = 0.001)] were observed only in the German group. Concern about possible underlying cancer was relatively common but without significant difference between the 2 groups (5/48 vs. 11/45; P = 0.10). Biliary obstruction was an indication for surgery in both groups (6/48 vs. 3/45; P = 0.31). Two patients in each group had pancreas divisum as a potential cause of CP.

Preoperative Duration of Symptoms and Indications for Surgical Intervention

The principal indication for operation in the 93 patients is shown in Table 3. In 2 patients from the US center and in 7 patients in the German collective there were multiple indications for intervention.

Chronic pain was the most frequent symptom in both groups. Portal/mesenteric vein thrombosis with consequent portal hypertension leading to formation of extensive collaterals and splenic vein occlusion with consequent left-sided portal hypertension were also much more prevalent in the German group.

Preoperative data were unavailable in the US group regarding CBD-stenosis in 2 patients.

Biliary stenosis/jaundice

CBD indicates common bile duct; SMV, superior mesenteric vein; PV, portal vein.


TABLE 3. Principal Indication for Surgical Treatment in 93 Patients With CP

<table>
<thead>
<tr>
<th>Indication</th>
<th>Germany</th>
<th>United States</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic pain</td>
<td>15 (31%)</td>
<td>28 (62%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Suspicion of malignancy</td>
<td>5 (10%)</td>
<td>11 (24%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Gastric outlet obstruction</td>
<td>8 (17%)</td>
<td>1 (2%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>7 (15%)</td>
<td>0%</td>
<td>0.01</td>
</tr>
<tr>
<td>Biliary stenosis/jaundice</td>
<td>6 (13%)</td>
<td>3 (7%)</td>
<td>0.31</td>
</tr>
<tr>
<td>Multiple indications</td>
<td>7 (15%)</td>
<td>2 (4%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Surgical Interventions

The choice of surgical therapy differed greatly between the 2 centers. The technique of pancreatectomy used in the US center typically was a classic pancreatectoduodenectomy (with antrectomy), whereas the pylorus-preserving technique was preferred for pancreatectoduodenectomy in the German group (Table 5). Of greater interest, more than half of the German patients had a duodenum-preserving pancreatic head resection versus none in the US group. Less commonly performed were distal pancreatic resections or pure drainage procedures.
TABLE 4. Subgroup Analysis of the Head Size and Complications of German Patients Operated Upon Within 3 Yr of Onset of Symptoms or Later

<table>
<thead>
<tr>
<th></th>
<th>&lt;3 yr (n = 48)</th>
<th>&gt;3 yr (n = 45)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>21</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Average time after onset</td>
<td>12.67 ± 10.6 mo</td>
<td>9.22 ± 50.48 mo</td>
<td>n.s.</td>
</tr>
<tr>
<td>Size of pancreatic head</td>
<td>4.62 ± 1.26 cm</td>
<td>4.58 ± 1.15 cm</td>
<td>n.s.</td>
</tr>
<tr>
<td>DHC stenosis</td>
<td>29%</td>
<td>52%</td>
<td>0.11</td>
</tr>
<tr>
<td>Gastric outlet obstruction</td>
<td>24%</td>
<td>12%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>14%</td>
<td>8%</td>
<td>n.s.</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>48%</td>
<td>32%</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Student t-test, *P* < 0.05 was considered statistically significant; 2 patients were lost to follow-up and were excluded from this analysis.

TABLE 5. Treatment Performed in 93 Patients

<table>
<thead>
<tr>
<th>Operation</th>
<th>Germany (n = 48)</th>
<th>United States (n = 45)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreaticoduodenectomy with antrectomy (whipple)</td>
<td>1 (2%)</td>
<td>37 (82%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pylorus-preserving pancreaticoduodenectomy (PPPD)</td>
<td>8 (17%)</td>
<td>3 (7%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Duodenum-preserving pancreatic head resection (DPPHR)</td>
<td>25 (52%)</td>
<td>None</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Distal pancreatectomy</td>
<td>5 (10%)</td>
<td>3 (7%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Others*</td>
<td>9 (19%)</td>
<td>2 (4%)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Six patients in the German group had no surgical or interventional treatment (see text).

DISCUSSION

CP comprises a wide spectrum of disorders ranging from “minimal change disease” presenting with pain all the way to advanced fibrotic destruction of the gland with resulting exocrine and endocrine failure and complications involving biliary, duodenal, or spleno-portal venous obstruction. In part because of the variability of the manifestations and probably in part related to subjective criteria used by physicians and surgeons, there is no agreement on the principles or guidelines to provide consensus guidelines that can rationalize surgical treatment.

If, however, there are genuine differences in the morphology of CP in various geographic locales, as exemplified by our findings at these 2 centers, these may reflect as yet undetermined differences in pathogenesis. European studies, following the lead of Beger et al., have in recent decades focused on the phenomenon of the pancreatic head mass in CP, whereas American investigators have either not observed this inflammatory mass, ignored it, or have seen it much less frequently. That difference led to the hypothesis that initiated this collaboration.

In this study, we did indeed find an important difference in the median anterior-posterior diameter of the pancreatic head: 4.5 versus 2.6 cm. Apart from the Hamburg group, the other European randomized trials of the Beger and Frey operations did not routinely quantify the size of the pancreatic head. Izbicki et al. reported that the inflammatory mass was greater than 5 cm in 84% of their patients, a size essentially identical to that in our Freiburg group. In a later study, Izbicki’s group reported that all patients had an enlargement of the pancreatic head averaging 56 mm. Presumably as a consequence of the changes in the pancreatic head, obstruction of the bile duct, duodenum, and major intrapancreatic veins occurred more frequently in the Freiburg patients although pain and functional insufficiency were no different. The cause for the presence or absence of the pancreatic head mass in CP, and therefore, the basis for the difference between our German and American patients, remains a matter of speculation.

There was a significantly longer duration of prepneumoperative symptoms (5 vs. 2 years) in the Freiburg patients; however, as shown in Table 4, that difference in time to intervention did not lead to further enlargement of the pancreatic head nor explain its functional consequences. Although surgical drainage of the pancreatic duct has been shown to be more effective than endoscopic treatment of pain in CP, the lack of consensus on the optimal time for surgical treatment may be reflected in the relative delay of referral to the German surgeons. Differences in consumption of alcohol and anatomic variations such as pancreas divisum were not apparent among our patients, but one could speculate whether autoimmune CP, which causes enlargement of the pancreatic head, might be more prevalent among patients operated upon for complications of CP in Germany than in the United States.

The enlargement of the pancreatic head would seem to direct German surgeons to use the duodenum-preserving head resection. This is especially so when CP is complicated by portal hypertension caused by mesenterico-portal venous obstruction. In that circumstance a pancreateoduodenectomy (Whipple-type operation) may be impossible without the risk of potentially lethal hemorrhage, but the partial head resection can be accomplished with relative safety, especially if portal flow can be restored. Nonetheless most American surgeons continue to prefer the pancreateoduodenectomy, with or without preservation of the antrum and pylorus, despite European studies that demonstrate the efficacy of the duodenum-preserving operations in the management of pain with equal or perhaps
lower morbidity.12,22,27,28,29 Recent updates in fact show no long-
term differences between pancreatoduodenectomy and the duode-
num-preserving head resections with respect to long-term pain
control or exocrine/endocrine function.31,37 Suspicion of possible
underlying cancer was not significantly different in the 2 groups and
did not seem to influence the choice of operation.

There are published observations that the natural history of
CP includes the possibility of spontaneous subsidence of pain at the
time of “burn-out” of the gland with exocrine/endocrine failure.14 This is an attractive outcome for physicians and gas-
troenterologists who try to avoid subjecting their patients to the
perceived risks of surgery and may underlie the extra delay of
referral in Freiburg. However, the hoped-for burn-out does not
occur for many years at best,17 and it is reported that more than
half of patients are still in pain after 10 years of medical
management.3 Although our study suggests the possibility that
prolonged waiting may incur greater risk of additional compli-
cations due to advancing morphologic changes, there are still no
accepted guidelines or standards which define the failure of
nonoperative therapy—how long to persist, what limit to anal-
egize treatment, how much disruption of normal life.37

Ten years after the American Gastroenterological Association
called for testing of surgical versus nonsurgical therapy for CP,11
randomized controlled trials show the superiority of surgical resec-
tion over endoscopic methods.32,33 Which operation to use, how-
ever, may continue to reflect valid institutional or regional prefer-
ences and the dictates of as yet not understood differences in
pancreatic morphology.40

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