Gallstone Pancreatitis

Biliary Tract Pathology in Relation to Time of Operation

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During a 29-month trial, 65 patients with acute gallstone pancreatitis were randomly selected for biliary tract explorations either within 73 hours of admission (36 patients) or at three months following remission with nonoperative measures (29 patients, with five others awaiting elective operation). The details of surgery were identical, *i.e.*, cholecystectomy, transduodenal sphincteroplasty, and pancreatic duct septotomy. Major bile ducts were cleared of stones by Fogarty catheter passage up the sphincteroplasty. At early operation, pancreatitis was in the acute edematous form in 29 patients, necrotizing in six, and hemorrhagic in one. Acute inflammatory changes were also noticed in three patients who underwent late operation. The locations of the gallstones in patients undergoing early versus delayed operations were, respectively: 97% and 100% in gallbladder, 75% and 28% within common or hepatic ducts ($p < 0.02$), and 31% and 0% free in duodenum ($p < 0.01$). The distal choledochus and ampulla were inflamed in 89% of the patients who underwent early operations, but in merely 17% operated upon electively ($p < 0.01$). Concomitant acute cholecystitis was present in 31% of the patients if surgery was performed during the initial admission, but in only 3% of the patients at delayed operation ($p < 0.05$). Most striking was the sudden "gush" of pancreatic juice when the ampullary sphincter was first stretched or cut during sphincteroplasty at early operation. Precipitous falls in serum amylase levels then followed over the next 24 hours. No significant differences were noticed in the mortality rate (one death after early operation, two after a delayed procedure), major morbidity rate (in four and three patients, respectively), or in duration of the initial hospitalization period (early operation: 13.5 days, delayed operation: 16.7 days). However, a second admission to the hospital for the delayed operation (12.1 days) was avoided by early operation. These data support the concept that biliary pancreatitis is probably initiated by gallstone passage through, or lodgement at, the ampulla of Vater. The resultant ampullary edema with or without gallstone impaction appears to be the anatomic cause for major pancreatic duct obstruction and the consequent pancreatitis. Early and appropriate surgical relief of the biliary tract pathology via a transduodenal sphincteroplasty can obviate the need for a second admission to the hospital without increasing, significantly, the attendant morbidity and mortality rates.

ALTHOUGH AN ASSOCIATION between biliary tract disease and pancreatitis was first recorded in 1901,[9] little in the way of additional insight as to the mechanism of origin for pancreatic inflammation was uncovered until Acosta and co-workers noticed that gallstone passage into the intestinal tract often coincided with the initial symptoms of pancreatitis.[1] These episodes of so-called biliary pancreatitis have almost always evolved in the absence of alcohol ingestion.[1,7,14] Since a gallstone impacted in the terminal common bile duct has seldom been found whenever an operation is performed within one or two days of disease onset, and since pancreatic inflammation may continue and even significantly worsen despite passage of the gallstone, the exact event responsible for inciting nonalcohol-related acute pancreatitis has remained somewhat of a mystery.

Ignorance on our part, however, may well be due to a deliberate and almost universal policy to abstain from opening the duodenum, as well as to avoid manipulation of the ampulla at the time of an acute attack.[6–8,11] Accordingly, rarely, if ever, during an acute bout have the terminal pancreatic and common bile ducts been directly inspected and, thus, the pathologic features of the supposedly initiating anatomic area are recorded in sufficient detail during the phase of acute inflammation. This gap in our knowledge is, similarly, reflected by a failure to perfect an appropriate operative procedure which not only will reverse the progression of acute gallstone-associated pancreatitis, but which also will limit significantly the likelihood of recurrent episodes.[3,5,7,13]

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Proposed Study

In order to better define the pathologic anatomy of the biliary tract, and especially its terminal, ampullary end, both operative cholangiography and transduodenal sphincteroplasty seem to be indicated. At the same time, entry of the main pancreatic duct could be identified for determination of exact anatomic location and associated inflammatory changes. The presence and location of gallstones might then be recorded as well. If surgery was performed either shortly after admission to the hospital for treatment of an acute attack or several months later, following successful nonoperative management, differences in observed pathologic features and gallstone presence might then explain many of the discrepancies in theory of origin, specific surgical procedure, optimal time for operation, and cause for recurrent attacks.

Provided that the operation itself was one for which there was general acceptance as a method for management of gallstone pancreatitis, it was not believed necessary to gain approval by a Clinical Trials Committee, but instead only patient compliance via an informed surgical consent. The same contention seemed reasonable with respect to urgent or delayed time of operation.

Protocol

All patients admitted to the Trauma Service of Grady Memorial Hospital with a clinical presentation consistent with an acute episode of biliary pancreatitis automatically became candidates for study. The diagnosis of gallstone-induced acute pancreatitis was made on the basis of: 1) abdominal symptoms and signs of acute pancreatic inflammation (*i.e.*, upper abdominal pain and tenderness, abdominal distension, hypoactive to absent peristalsis, and mild to moderate dehydration); 2) hyperamylasemia and/or hyperamylasuria; and 3) a reliable recent history of abstinence from alcohol.

Documented prior episodes of biliary colic, acute cholecystitis, or operations on the biliary tract as well as mild elevations of the serum bilirubin level were considered to be items which increased the accuracy of the clinical diagnosis, yet never were such findings made absolute criteria for patient inclusion in the study. Specific confirmatory tests were obtained whenever practical and possible. These included an oral gallbladder x-ray series once the acute attack had subsided, intravenous cholangiography, radionuclide excretion scan, biliary sonography, and upper abdominal computerized axial tomography.

Operation

The operation performed was standardized as to details in technique. Only the time selected for operation varied. Through a right subcostal incision, the abdomen was first explored, with special notice being taken of the severity of associated pancreatic inflammation. Following cholecystectomy, an operative cholangiogram was obtained through catheter cannulation of the cystic duct stump. After the cholangiocatheter had been withdrawn, a biliary Fogarty catheter was passed down the cystic duct, into the common duct, and then through the ampulla into the duodenum. By inflation of the Fogarty balloon followed by traction on the catheter hub, the exact level of the ampulla could be determined with considerable accuracy. With the coagulation current, a transverse duodenotomy was appropriately made. The ampulla was readily identified by the protrusion of the Fogarty catheter. The tip of the catheter was grasped with an Adson clamp, and the clamp was then drawn up into the ampulla by traction on the hub end of the Fogarty catheter. With the Adson clamp opened, a sphincterotomy was performed with the coagulation current for a distance of 2.0 to 2.5 cm along the anterolateral course of the common bile duct. Conversion of the sphincterotomy into a sphincteroplasty was accomplished by approximation of the contiguous walls of duodenum and common duct with interrupted sutures of polyglycolic acid. The pancreatic duct was next identified, cannulated with mosquito forcep, the forcep opened, and a septotomy of the terminal 1.0 cm of pancreatic duct was done in a manner similar to the sphincterotomy of the common duct. Nevertheless, the pancreatic duct septotomy was never sutured to close the mucosal edges.

Once the sphincteroplasty and septotomy had been completed, the Fogarty catheter was withdrawn from the cystic duct, and the cystic duct ligated. The Fogarty catheter was then introduced from below via the sphincteroplasty up into the common bile duct, to clear the biliary tree of residual stones. Following removal of the Fogarty catheter, the duodenotomy was closed in two layers, transversely. T-tube decompression of the common bile duct and external drainage of the abdomen were routinely omitted.

Randomization

Time of operation was determined by the final digit in the patient's previously randomly assigned hospital number. An odd digit dictated early operation, that is, within 72 hours of admission to the hospital; while an even number prescribed routine supportive care, with readmission to the hospital in three to six months for the same operation to be performed electively.

With respect to antimicrobial therapy, all patients received 2 g of cefamandole intravenously every six hours for five days during the initial period of hospi-

talization. When operation was performed at a subsequent admission to the hospital, the same antibiotic was given perioperatively in 2 g aliquots as a prophylactic measure.

In addition to gross pathologic changes being noticed at operation, patients were also evaluated according to standard liver function tests, the aforestated radiographic and sonographic procesures, clinical course for study related hospitalizations, and subsequent symptoms potentially caused by a recurrent episode of acute pancreatitis. Special notice was made of fluctuations in the serum amylase levels following early versus late operations, and correlation of such with the postoperative clinical assessment as to remission or progression of the pancreatitis.

Results

During the 29-month interval between November 1, 1978 and March 31, 1981, 65 patients were admitted to the Trauma Service of Grady Memorial Hospital with a clinical diagnosis of acute gallstone pancreatitis. According to an odd final digit in the hospital number, 36 patients were randomly selected to undergo early operation, that is, within 17–73 hours of admission to the hospital. The remaining 34 patients had an even final digit in their hospital number and were, thereby, allocated to supportive care alone, with the same operation to be performed electively no sooner than three months after discharge from the hospital. Of the latter group, 29 patients have undergone the delayed operative procedure, with the final five awaiting readmission to the hospital.

There were 51 black patients and 14 whites, 54 females and 11 males. The patients ranged in age from 16 to 83 years, with an average of 59 years. Alcohol abuse at some time in the distant past was acknowledged by two patients. Obesity was noticed in 43 patients, while two patients appeared to be wasted. Each of the females had had at least one pregnancy. A prior episode of acute abdominal disease, consistent with an attack of pancreatitis, had been experienced by 43 patients. Six of these patients had undergone an operation on their upper abdomen previously, one being a cholecystectomy. There were no significant differences in such patient profile data between the two groups, *i.e.*, early versus delayed operation.

The initial serum amylase levels varied between 37 and 28,200 units, with an average of 1,158 units (Table 1). Other pertinent laboratory data were within the expected ranges for patients experiencing an attack of biliary pancreatitis. The highest serum bilirubin level was 5.4 mg/dl, yet the average for the entire patient population was only 1.8 mg/dl.

TABLE 1. *Laboratory Profile (Average Values on Initial Hospitalization)*

	Range of Laboratory Values	Early Operation	Late Operation
Serum amylase	37–28,200 units	1211	1093
Total bilirubin	0.7–5.4 mg/dl	1.9	1.7
Serum calcium	7.9–10.1 mg/dl	9.1	9.3
SGOT	43–327 units	173	203
White blood count	5.6–23.4 $10^3/mm^3$	12.9	13.7

On more specific study of the biliary tract and pancreas, the gallbladder failed to appear on radionuclide scan in 38% of the patients, and on intravenous cholangiographic examination in 46%, when such were run during the initial hospitalization period (Table 2). Gallstones could be detected on sonographic examination in 93% of the patients. Computerized axial tomography confirmed pancreatic enlargement in each of the 16 patients so studied.

Severity of the Pancreatitis

Pathologic grading of the pancreatitis noticed during early operation was acute edematous in 29 patients, necrotizing in six, and hemorrhagic in one. In cases of delayed operation, a thickened gland was noticed in 22 patients, acute inflammation in five, and a seemingly normal pancreas in two.

Operative Cholangiography

Common bile duct stones were noticed on 64% of the operative cholangiograms obtained at early operation, but in only 18% of those performed during the delayed procedure (Table 3). Dye usually flowed freely into the duodenum, but rarely did the pancreatic duct become visible. In only one patient, undergoing early operation, was there reflux of dye into the pancreatic duct, and in this instance all signs and symptoms of acute pancrea-

TABLE 2. *Specific Diagnostic Studies on Initial Hospitalization*

	Early Operation	Late Operation
Radionuclide excretion scan	15	11
GB visualized	9	7
CBD visualized	14	10
Intravenous cholangiogram	16	8
GB visualized	7	6
CBD visualized	1	0
Sonography	33	25
gallstones	31	23
enlarged pancreas	30	20
Computerized axial tomography	9	7
enlarged pancreas	9	7
dilated bile ducts	1	0

TABLE 3. *Operative Cholangiogram (Interpretation in Biliary Pancreatitis)*

	Early Operation		Late Operation	
	Number	Incidence (Per Cent)	Number	Incidence (Per Cent)
Patients studied	33	—	28	—
Common duct stones	21	64	5	18
Dye into duodenum	28	85	27	96
Pancreatic duct visualized	1*	3	4	14

* All symptoms and signs of an acute process had subsided.

titis had subsided, despite a persistence of mild pancreatic edema.

Biliary Tract Pathology

Stones were noticed in the gallbladder of all patients except the one who underwent cholecystectomy at a previous admission (Table 4). However, common bile duct stones were retrieved in 75% of those patients who underwent early operation, in contrast to only 28% of the patients who had delayed procedure. Gallstones were found free within the duodenum, usually in the third or fourth portion, in 31% of the patients if operation had been performed during the acute episode; never were stones discovered in the duodenum at the late operation. In contrast to the findings reported by Acosta,[1] only two patients who underwent early surgery had stones impacted in the ampulla.

Acute cholecystitis was present in 31% of the patients who underwent early operation, but in only 3% if operation had been randomized to a later admission (Table 5). Inflammation of the ampulla, terminal common bile duct, and/or duodenum was a striking feature in 89% of the patients when surgical exploration was performed during the acute attack. By contrast, such inflammatory changes were noticed in only 17% of the patients having the elective procedures at a later date.

Probably the most striking feature of all, however, was a sudden gush of clear pancreatic juice flowing through the dilated or cut ampulla when operation was performed during an episode of acute inflammation. The only exception at early operation was a patient whose signs and symptoms of acute pancreatitis had already subsided prior to the operation. A similar brisk flow of pancreatic juice was noticed in three patients who underwent elective operations at a later period of hospitalization, but two of these three patients had gross pathologic changes of acute, edematous pancreatitis.

Without exception, the pancreatic duct emptied into the terminal 0.5 cm of common bile duct within the ampullary channel. This was true for all patients, whether surgery was performed early or late.

TABLE 4. *Operative Findings in Biliary Pancreatitis (Location of Gallstones)*

	Early Operation		Late Operation	
	Number	Incidence (Per Cent)	Number	Incidence (Per Cent)
Patients	36		29	
Gallbladder	35*	97	29	100
Common duct	27	75	8	28
Duodenum	11	31	0	—

* Single exception accounted for by prior cholecystectomy.

TABLE 5. *Operative Findings in Biliary Pancreatitis (Inflammation or Scar)*

	Early Operation		Late Operation	
	Number	Incidence (Per Cent)	Number	Incidence (Per Cent)
Patients	36		29	
Acute cholecystitis	11	31	1	3
Distal common duct inflammation	32	89	5	17
scar	10	28	6	21
Duodenal inflammation	7	19	1	3

Postoperative Serum Amylase

When surgery was performed during the initial hospitalization period, serum amylase values fell precipitously to 35% of admission levels within 24 hours after operation (Table 6). By the fourth to sixth day after operation, these values were down to 9% of those originally reported and somewhat below the upper limit of normal hospital standards. If, on the other hand, operation had been performed electively on a second hospitalization, admission determinations of the serum amylase levels were in the same range as those obtained on the fourth to sixth day after operation for patients having the early operation. Instead of a decline in serum amylase levels, the values were almost doubled by the end of the first day after operation, yet these returned to the normal range within three to five days, thereafter.

Clinical Response

No patient who underwent an early surgical procedure had a worsening of the clinical course. In fact, just the opposite, rapid amelerioration of signs and symptoms, was common. Although hyperamylasemia did develop, transiently, following the delayed operation in most patients, never was a true recurrent episode of pancreatitis believed to have been precipitated. On fol-

TABLE 6. *Follow-up Serum Amylase (Average Values During Hospitalization for Operation)*

	Early Operation	Late Operation
Patients studied	23	11
On admission	1,793	163
Postoperation Day 1	621	304
Postoperation Days 4–6	159	127

low-up examination of one to 30 months (average: 14.3), not patient who underwent operation had developed recurrence of pancreatitis.

Complications/Deaths

Twelve specific complications developed in six of the patients after operation (Table 7). Infection of the incision and/or subphrenic space accounted for seven of these complications. The single duodenal fistula appeared to be the result of abscess erosion through the duodenotomy suture line some four weeks after operation.

Three patients died—two quite suddenly, as a complication of massive pulmonary embolism. The origin for a fatal septicemia could never be found, even after autopsy examination, in an elderly female.

There was no significant difference in the morbidity or mortality rates on comparison of the two groups, established by time of operation. The overall mortality rate was 5%, with incidence of a major complication being 9%.

Duration of Hospital Stay

The average hospital stay for those patients surviving the initial admission to the hospital was 13.5 days if the operation was performed at the early date, and 10.7 days if only supportive care was given. The second period of hospitalization averaged 12.1 days when operation had been delayed. Although a difference of 2.8 days was not significant between the two groups with respect to the initial admission to the hospital, total hospital days for both categories of 13.5 and 22.8 gave a highly significant difference ($p < 0.01$) of 9.3 days. Expressed in terms of a *per diem* ward rate of $120.00, the difference amounted to $1,116.00 per patient in extra hospital costs, exclusive of laboratory and medical fees, if operation was delayed until a second admission to the hospital.

TABLE 7. *Complications of Operation*

	Early Operation	Late Operation
Patients	36	29
Subphrenic abscess	2	2
Wound infection	2	1
Duodenal fistula	—	1
Phlebitis/bacteremia	1	—
Pulmonary embolism	1*	1*
Septicemia of unknown origin	—	1*
None	33	26

* Cause of death.

Discussion

An association with gallstone impaction in the terminal common bile duct or passage of a gallstone into the intestinal tract can be shown to exist in at least one-third of the patients who present with inflammatory disease of the pancreas.[1,7,9,10,12] Direct inspection of the ampulla of Vater in such cases of acute biliary pancreatitis has consistently revealed an edematous papilla of Vater,[12] intense inflammation of the distal common bile duct, and what appears to be a resultant obstruction of the pancreatic duct as it terminates in a common channel with the major bile duct. Certainly, the sudden escape of pancreatic juice when the sphincter is dilated or cut in these cases of acute pancreatic inflammation, and the consistent anatomic union of the pancreatic duct along the terminal 0.5 cm of common bile duct, appear to confirm this assumption. At a time when pancreatic inflammation has resolved, an angry distal choledochus and significant ampullary edema are seldom noticed. In addition, sphincter dilation or division generally fails to produce the same "gush" of pancreatic juice.

Operative cholangiograms rarely demonstrate dye reflux into the pancreatic duct if surgery is performed during an acute attack, even though there may be a free flow of contrast material into the duodenum. However, it is ampullary sphincter division or dilation, not pancreatic duct septotomy, which permits the sudden escape of pancreatic juice under what appears to be a slight increase in pressure. The obstruction, itself, has seemed to be caused more by ampullary edema than by true scar tissue.

Gallstone passage through the sphincter is probably the single event which most commonly leads to ampullary edema.[1] Gallstones can usually be recovered from

TABLE 8. *Recurrence of Biliary Pancreatitis (Without Operation on Biliary Tract)*

Author	Year	Patients	Died	Mortality Rate	Recurrence	Incidence Rate
Elfstrom[4]	1978	63	0	—	16	25%
Kelly[7]	1980	14	1	7%	5	36%

TABLE 9. *Recurrence of Biliary Pancreatitis (Following Operation on Biliary Tract)*

Authors	Year	Patients	Sphincterotomy/ Sphincteroplasty	Follow-up (Range)	Recurrent Pancreatitis	Incidence of Recurrence (Per Cent)
Albo, et al.[2]	1963	15	No	3.5 years (0–7)	0	—
Kelly[7]	1974	52	No	5 years (1–15)	2	4
Dixon and Hillam[3]	1970	62	No	5 years (1–10)	5	8
Sanchez-Ubeda, et al.[13]	1956	25	No	5.5 years (1–11)	2	8
Glenn and Frey[5]	1964	119	9	15 years (1–30)	34	29
		49	No	17.4 years (5–30)	23	47

the stool of such patients, stones may even be found in the duodenum, and residual common duct gallstones tend to be small and located well above the ampulla. These facts add further support to the idea that the gallstone causing injury to the ampulla (and thus the stone which has incited the pancreatitis-inducing ampullary edema) has already passed into the intestinal tract.

Common duct exploration during an acute episode of pancreatitis only removes those stones which might be the agents for inciting a future attack. Little if any benefit is obtained for reversal of the present bout of acute pancreatitis. Likewise, pancreatic drainage, common duct decompression via cholecystotomy or T-tube insertion, and tube jejunostomy also failed to relieve the obstruction created by an edematous ampulla or an impacted gallstone.[1,6–8,10–12] Only sphincterotomy or sphincteroplasty appear to reverse the pathologic chain of events which block the free flow of pancreatic juice. A formal approach to sphincteroplasty or perhaps a resort to endoscopic sphincterotomy would seem to offer the greatest promise for an immediate remission.[12]

Failure to at least in part correct the biliary tract pathology consistently leads to a high incidence of recurrent pancreatitis (Table 8).[4,7] However, common bile duct stones tend to reform even though the gallbladder has been removed. Longer follow-up periods clearly demonstrate the propensity for biliary pancreatitis to recur as new stones form and are passed through the ampulla (Table 9).[2,3,4,5,13] If, instead, an operation is used which will almost guarantee the unrestricted passage of gallstones down the common duct and out into the intestinal tract, then recurrent episodes might be eliminated almost altogether. A generous transduodenal sphincteroplasty seems to offer just such a solution. Only long-term follow-up study will confirm the reliability of this approach.

Finally, there remains the question as to when operation should be performed.[1,6–8,10–12] Past experience has dictated that the mortality rate is unacceptably high if surgery is performed during an acute episode of biliary pancreatitis, yet it would appear that the operative procedures previously chosen have in no way corrected the obstructive ampullary edema. Historically, the wrong operation has rarely if ever given immediate or long-term patient benefit.

The present study clearly demonstrates the equal safety of an early versus delayed operation. Additional savings in both time and money seem to give further merit to such an approach.

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