Appropriate Timing of Cholecystectomy in Patients Who Present With Moderate to Severe Gallstone-Associated Acute Pancreatitis With Peripancreatic Fluid Collections

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Summary Background Data: Standard management of gallstone-associated acute pancreatitis calls for cholecystectomy to be performed during the same hospitalization after acute symptoms have subsided. However, infectious complications are common when cholecystectomy is performed sooner than 3 weeks after severe acute pancreatitis. Fluid collections, common in patients with moderate to severe acute pancreatitis, are additionally problematic. No previous study has examined the role of peripancreatic fluid collections and subsequent pseudocyst in outcomes after cholecystectomy in these patients.

Objectives: We compare results of delaying cholecystectomy after moderate to severe acute pancreatitis with early cholecystectomy.

Methods: Since 1987, all patients with moderate to severe gallstone-associated acute pancreatitis and associated fluid collections were addressed. Moderate to severe acute pancreatitis was defined as > 5 Ranson prognostic indicators. Fluid collection was established by computed tomography (CT) scan. Patients were evaluated for duration of hospitalization, complications of cholecystectomy, resolution or persistence of pseudocysts, nonoperative interventions performed on pseudocysts, intercurrent episodes of acute pancreatitis during the monitoring period, episodes of sepsis, and mortality.

Results: A total of 187 patients with moderate to severe gallstone-associated acute pancreatitis survived their acute stage; 151 had peripancreatic fluid collections. Seventy-eight of the 187 had early cholecystectomy, 62 of whom had fluid collections; 109 were monitored before cholecystectomy, 89 of whom had fluid collections. Fluid collections resolved without intervention in 36 (40%) of 89 in the monitored group and in 13 (21%) of 62 in the early cholecystectomy group. Percutaneous drainage was performed in 16 (18%) of 89 in the monitored group and in 31 (50%) of 62 in the early cholecystectomy group. Sepsis occurred in 6 (7%) of 89 in the monitored group and 29 (47%) of 62 in the early cholecystectomy group. Complications of cholecystectomy occurred in 6 (5.5%) of 109 of the monitored patients and in 34 (44%) of 78 in the early cholecystectomy group. Fifty-three patients in the monitored group and 49 patients in the early cholecystectomy group required operative pseudocyst-enterostomy. This procedure was combined with cholecystectomy in the monitored patients. Mean hospitalization was longer in the early operation group.

Conclusion: Cholecystectomy should be delayed in patients who survive an episode of moderate to severe acute biliary pancreatitis and demonstrate peripancreatic fluid collections or pseudocysts until the pseudocysts either resolve or persist beyond 6 weeks, at which time pseudocyst drainage can safely be combined with cholecystectomy.


The literature regarding patients who sustain an episode of moderate to severe acute pancreatitis primarily focuses on the critical care aspects of management in these patients. As these management principles have been perfected, the survival rates for moderate to severe acute pancreatitis have improved progressively. In gallstone-related acute pancreatitis, cholecystectomy is performed after resolution of the acute event to prevent subsequent episodes. Cholecystectomy is performed during the same hospitalization. Our report focuses on patients who have had moderate to severe acute pancreatitis caused by gallstones. These patients must recover from the acute critical care component of their pancreatitis before undergoing a cholecystectomy. Patients who have recovered from moderate or severe acute pancreatitis uniformly harbor a recognized or at times unrecognized peripancreatic fluid collection. Although organized reviews of this issue are scant in the literature, we have become aware of risks arising when these fluid collections are either ignored or poorly managed. The timing of cholecystectomy in patients with peripancreatic fluid collections has not been determined. Early cholecystectomy raises the risk of a second general anesthetic or a risk of a second interventional procedure to manage persistent fluid collections. We additionally have encountered patients with an episode of moderate to severe acute pancreatitis who have had their cholecystectomy and are referred because of an apparent contamination of the peripancreatic fluid collection at time of that operation. These
patients may require urgent or emergent management of their peripancreatic fluid collection at a time in which it is still possible that the pseudocyst or fluid collection might have resolved spontaneously had it not been contaminated. In this circumstance, our concern is that early cholecystectomy not only failed to recognize the possibility that the pseudocyst would persist but actually exposed the cyst to contamination and sepsis thus forcing an early intervention in the pseudocyst.

It is generally agreed that any patient with an episode of moderate to severe acute pancreatitis should undergo early computed tomographic (CT) imaging. It is our experience that patients will be referred who have not had imaging performed and whose fluid collections simply have never been visualized. In patients whose fluid collections have been visualized, there are times in which a patient’s clinical improvement may be such that a repeat CT scan is not done. We believe patients should have confirmation of resolution of pseudocyst before cholecystectomy for the reasons mentioned. The literature regarding cholecystectomy has addressed a similar issue, the timing of cholecystectomy after severe acute pancreatitis evaluated in a retrospective fashion. These studies have documented that earlier operation for simple acute pancreatitis is safe while early operation after severe acute pancreatitis had an unacceptably high rate of infectious complications. These studies have not addressed the contribution made by peripancreatic fluid collections.

All surgeons essentially agree that gallstone-induced acute pancreatitis has a significant risk of recurrence after the first episode; therefore, prompt operative intervention is the norm. Naturally, this precept is often violated in patients with moderate to severe acute pancreatitis because so much time is spent in managing the patient’s acute episode. Thus the amount of delay before consideration for cholecystectomy is longer in a patient who has had this magnitude of an attack. Following this standard, a surgeon may feel obligated to proceed promptly to cholecystectomy after the patient has stabilized. We believe that this perceived urgency prompts surgeons and referring physicians to resort to cholecystectomy soon after symptom resolution. We are unaware of any literature regarding the risk of recurrence of acute pancreatitis after moderate to severe gallstone-induced pancreatitis.

Several studies have evaluated the evolution of fluid collections after acute pancreatitis. Spontaneous resolution of peripancreatic fluid collections and of pseudocyst has been documented. The frequency with which this may take place is highest in patients whose fluid collection accumulated early after an episode of acute pancreatitis compared with patients with chronic pancreatitis. Some patients never develop a true cyst with resolution of the fluid before a cyst can develop. Pseudocysts and fluid collections may be treated by percutaneous or endoscopic methods. The appropriate timing of these techniques has been reviewed carefully. These interventions in sterile collections may result in infected peripancreatic fluid collections. The complication of infection in the previously sterile peripancreatic fluid collection may force one to consider definitive operative management of the peripancreatic fluid collection at an earlier stage. In this case, the timing of cholecystectomy is further complicated by prematurely forcing pseudocyst management. It has been our management principle and the basis for our study that patients with moderate to severe acute pancreatitis and documented fluid collections be given a period of evaluation that takes place after the medical stabilization of their episode. Once the pseudocyst is found to resolve, then cholecystectomy is undertaken. If the pseudocyst persists, combined management of the gallbladder and the pseudocyst is performed simultaneously.

We have been interested over the years in assessing the behavior of pseudocyst and the influence that ductal anatomy may play in the behavior of pseudocyst. This information has been specifically applied to the successes of nonoperative measures such as percutaneous drainage in treating pseudocysts. As we have followed the current group of patients, we have examined ductal anatomy in those patients whose cysts persist. We are interested in the possibility that ductal anatomy may well predict those patients who have persistence of pseudocyst.

METHODS

Beginning in 1987, all patients with a diagnosis of moderate to severe acute pancreatitis induced by gallstones and found to have an associated peripancreatic fluid collection were evaluated. All patients were admitted to our hospital and provided the standard care for patients with this diagnosis. A battery of laboratory tests was obtained, including those pertinent to prognostic scales. Patients were stratified and defined as moderate to severe acute pancreatitis on the basis of Ranson’s prognostic indicators. Any patient with greater than 5 Ranson indicators was designated as moderate to severe acute pancreatitis. Each patient immediately underwent CT scanning. In those patients transferred into our institution without CT, scan this imaging was obtained as soon as possible after transfer. All patients were admitted to our intensive care unit (ICU).

Patients who required urgent operation and necrosectomy had simultaneous cholecystectomy and are excluded from this evaluation. All patients were monitored with repeat imaging to assess of persistence of fluid collection and the rate of spontaneous resolution over time of these fluid collections. Subset analysis was applied to the use of nonoperative measures to drain fluid collections that included percutaneous drainage or endoscopic drainage. Although many patients presented to our care with drains already in place, we used 2 primary indicators for utilizing percutaneous stents. Patients with infected pseudocysts were treated with urgent percutaneous drainage. In patients whose illness resulted in
significant nutritional and metabolic deficit, we performed percutaneous drainage to stabilize the patient and permit sufficient recovery to allow an elective operation with reduced risk to the patient. Note was made of patients who were managed with transpapillary drainage utilizing stents in the pancreatic duct. Episodes of infected fluid collections and pseudocysts that resulted from these measures were also monitored. The pseudocysts that persisted and required operative intervention were monitored for complications of that intervention and for success in permanently resolving pseudocyst in follow-up. Repeat CT scanning was used to determine resolution. In patients with percutaneous drains in place persistence of pseudocyst was defined as continued drainage of more than 150 mL/d of enzyme rich fluid. Specific attention was paid to the possibility of recurrent episodes of acute pancreatitis before cholecystectomy during the follow-up period in which pseudocyst or fluid collections were evaluated for spontaneous resolution.

All patients managed under our supervision from the start were included in a policy in which cholecystectomy was delayed until spontaneous resolution of pseudocyst or until persistence of pseudocyst was established. We define persistence in a pseudocyst still present more than 6 weeks after the initiation of the observation period. We define fluid collections as any fluid still apparent more than 1 week after initial presentation. Thus the total period of observation in our policy was of 7 weeks after the initial event in patients with moderate to severe acute pancreatitis. There were times in which a longer follow-up was required because of the medical status of each patient. Cholecystectomy was undertaken once spontaneous resolution of fluid collection or pseudocyst had taken place, even if this were sooner than 6 weeks. With pseudocysts that persisted beyond 6 weeks, a simultaneous cholecystectomy and operative management of the pseudocyst was undertaken during the evaluation period. The operative management preferred was cyst-jejunalostomy. ERCP and evaluation of ductal anatomy was obtained on all patients with persistent pseudocyst, and a previously described system for evaluating the abnormalities seen in the main pancreatic ductal anatomy in patients with pseudocysts was used.15,16

Patients who were managed with this policy were compared with patients who had cholecystectomy performed before resolution or established persistence of pseudocyst was determined. These patients were managed either at our institution by physicians not utilizing this policy or more often at outside institutions referred after having undergone early cholecystectomy. Specific attention was directed to complications of cholecystectomy including sepsis, length of hospitalization after cholecystectomy and need for a repeat general anesthesia after cholecystectomy. Reoperation and rehospitalization were assessed. Complications of the definitive pseudocyst management were evaluated. This included recurrence of pseudocyst, episodes of sepsis, infection, hemorrhage, and mortality. Length of hospitalization was also catalogued. Although not the focus of this report, we have assessed for any correlation between the ductal anatomy as evaluated by ERCP and the persistence of pseudocyst during the follow-up period. It should be noted that ERCP was not performed and ductal anatomy was not defined on patients who had spontaneous resolution of cysts; therefore, comparison cannot be made in this subset.

Differences in percentages were calculated using $x^2$ analysis and Fisher exact test where appropriate. $P$ values less than 0.05 were considered significant.

RESULTS

Since 1987, we have compared 187 patients with moderate to severe acute pancreatitis associated with gallstones. Using our criterion of fluid collections persisting more than 1 week after initial presentation, 151 (81%) of the 187 patients had fluid collections associated with moderate to severe acute pancreatitis. Nine patients with severe acute pancreatitis died in the early acute phase of disease and are not included in this study. Among these 187 patients, there were 78 who had an early cholecystectomy as their management before confirming possible resolution of their fluid collection; 62 of these 78 patients had fluid collections documented. The remaining 109 patients in the total population were managed by our formula of delayed cholecystectomy until resolution or established persistence of pseudocyst; 89 of these 109 patients had fluid collections defined in their early management. Among the 187 patients, 119 were female and 68 were male. The mean age was 39 years. Age and gender distribution was not different in the 2 groups under analysis. Although not documented well in each case, it is our estimate that 26 of the 187 patients had an episode of acute pancreatitis before the current episode presenting to our hospital. Interestingly and surprising to us, no patient in our group of patients whose cholecystectomy was delayed until resolution of pseudocyst had an episode of acute pancreatitis recur during this period of monitoring. The mean number of Ranson prognostic indicators was 7.9 ± 2.1 and was nearly identical in the 2 groups. Balthazar grading of CT scans was also comparable in the 2 groups.

Patients Undergoing Early Cholecystectomy

In our series, 78 patients underwent early cholecystectomy without regard to peripancreatic fluid collection; 41 of these 78 patients were referred from an outside institution, and 37 were managed entirely in our own institution. The 16 patients who had no persistent peripancreatic fluid collection were not evaluated further in this study. Among the remaining 62 patients, 31 (50%) had percutaneous drainage of their cyst. By initial report, the indication for percutaneous drainage in 29 of these 31 was for infected pseudocyst. After further evaluation, it was our finding that only 16 (55%) of
the 29 patients treated with percutaneous drainage for what was initially defined as infected cyst had infection before the drainage. Thirteen (45%) of the 29 patients who underwent early cholecystectomy had percutaneous drainage that was complicated by infection and sepsis. It was often this complication that prompted transfer to our care. The remaining 2 patients of the 31 had percutaneous drainage because of nutritional status and a need to provide time to stabilize the patient and to improve nutritional status. Thirteen patients underwent endoscopic transpapillary stent placement. All of these patients were in the early cholecystectomy group. Nine of 13 patients with no evidence of infected cyst before the stent placement sustained episodes of sepsis and apparently infected cysts after placement of the transpapillary stent. These 9 are included in the 29 patients who had percutaneous drainage that was performed as an urgent measure after developing sepsis. Thirteen of the 62 patients with early operation and persistent pseudocyst had resolution of their pseudocyst after their cholecystectomy. Six of those whose cyst resolved had been treated with percutaneous drainage, and 5 have both this modality and transpapillary drain placed. Reoperation after cholecystectomy was required in 49 of the 62 patients or 79% of patients. In each of these patients, the reoperation was definitive management of the pseudocyst. Excluding reoperation as a complication, patients with early cholecystectomy additionally sustained postoperative complication in 34 (44%) of 78 patients treated with early operation after recovering from an episode of moderate to severe acute pancreatitis. Sixteen of these 34 complications were infected pseudocysts arising as a consequence of early cholecystectomy. There was 1 death in the 78 patients treated with early cholecystectomy, for a rate of 1.3%.

Length of hospitalization was unpredictable because of the variable length of care before resolution of the acute process. Average length of stay for the patients with early cholecystectomy was 37.9 ± 9.2 days. If we focus on the length of hospitalization after release from the ICU, the length of hospitalization remaining was 20.1 ± 7.1 days in the patients with early operation. Rehospitalization for the patients with early cholecystectomy was necessary in 49 of 78 patients; 31 of these 49 patients requiring rehospitalization required more than 1 rehospitalization. Among the 49 patients who required operative management of pseudocyst, 4 patients (8%) had postoperative complications. Length of hospitalization after definitive operative management of pseudocyst was 6.9 ± 2.1 days. Follow-up imaging was obtained in 37 of the 49 patients treated with operative pseudocyst drainage. There were no pseudocyst recurrences identified in these 37 patients with a mean follow-up of approximately 16 months; 24 of these 37 had operative management. The remaining 13 were those whose pseudocyst resolved without further intervention.

### Delayed Cholecystectomy and Pseudocyst Monitoring

A total of 109 patients were assigned to management utilizing a policy of serial monitoring of fluid collections with cholecystectomy delayed until spontaneous resolution or established persistence of the fluid collections. Among these 109 patients, 89 had fluid collections. Among these 89 patients 36 (40%) had spontaneous resolution of their fluid collection during the monitoring period. These data are summarized in Table 1 and compared with data pertaining to patients who had early cholecystectomy. The mean length of time required for resolution of their fluid collection was 19.6 ± 3.1 days. Spontaneous resolution was established by repeat CT scanning. Patients who were followed in this manner underwent a mean of 3.6 ± 1.2 CT scans during their monitoring period. Thirty-six of the patients in the delayed cholecystectomy group were referred from outside institutions, and 73 were managed from within our own institution. No patient in the delayed cholecystectomy group required more than 1 operative procedure. Six of the patients who were referred from outside institutions had percutaneous drainage of an infected pseudocyst performed at their original hospital. On reviewing records it was suspicious that 3 of these cysts were not infected before placement of the percutaneous drain. An additional 10 of the patients transferred from an outside institution underwent percutaneous drainage at our institution to serve as a bridge to definitive operative procedure because of the debilitated state of the patients at the time of transfer. This offered an opportunity to enhance nutritional status and to stabilize any metabolic derangements that had taken place during the interval from the original attack to transfer to our facility. Thus 16 of the 89 patients in the category treated with delayed cholecystectomy had per-

| TABLE 1. Frequency of Fluid Collections and Frequency of Spontaneous Resolution of Fluid Collections in Patients Managed With Early Cholecystectomy Compared With Patients Monitored and Undergoing Delayed Cholecystectomy |
|-----------------|-----------------|-----------------|
| Patients assigned to undergo a policy of serial monitoring of pseudocyst | 109 | 89/109 (81%) (Pre-op) 36/89 (40%) |
| Patients managed with early cholecystectomy | 78 | 62/78 (79%) (Post-op) 13/62 (21%) |
cutaneous drainage placed. Table 2 summarizes the percutaneous drain usage in the early cholecystectomy group compared with the patients whose operation was delayed. Clinical sepsis occurred in 6 of the 89 patients in the monitored group. Each of these had percutaneous drainage placed before transfer to our institution.

There were 6 postoperative complications among the 109 patients who underwent delayed cholecystectomy. Laparoscopic cholecystectomy alone was performed in 56 patients. There were no complications in this group. The pseudocyst persisted in 53 of the original 89 patients with peripancreatic fluid collections, and these patients were managed with an open laparotomy and a combined cholecystectomy and cystenterostomy; 6 of these 53 patients' courses were complicated by wound infection managed by wound care. There were no deaths in patients managed by delayed cholecystectomy. Transpapillary stents were not used in any of the 109 patients treated with serial evaluation and delayed cholecystectomy. Follow-up CT scans were obtained in 47 of the 53 managed with combined cholecystectomy and cystenterostomy. Each of these patients had complete resolution of their pseudocyst by follow-up CT scan. All patients who had operative drainage of pseudocyst were symptom free in follow-up. Surprisingly, there were no episodes of recurrent acute pancreatitis in the patients followed and treated with delayed cholecystectomy after resolution or persistence of cyst.

The majority of patients with delayed cholecystectomy underwent their serial monitoring as outpatients. Thus the length of hospitalization for the patients who were managed by serial monitoring after clearance from their critical care for moderate to severe acute pancreatitis was $9.2 \pm 3.1$ days. The mean length of hospitalization for the readmission and cholecystectomy with or without pseudocyst drainage was $5.1 \pm 2.9$ days. These data were variable because of the mix of patients who had cholecystectomy alone versus those who had a more complex procedure. The hospitalization for the patients readmitted for a cholecystectomy was $1.2 \pm 0.1$ days. The length of hospitalization for patients managed with combined cholecystectomy and cyst enterostomy was $7.6 \pm 2.3$ days. Rehospitalization was thus necessary in all 109 patients managed by delayed cholecystectomy. Table 3 delineates a comparison between patients managed by a policy of monitoring of fluid collections compared with patients who underwent early cholecystectomy regarding reoperation, rehospitalization, and postoperative complications. Table 4 compares early cholecystectomy patients to delayed cholecystectomy regarding length of hospitalization, hospitalization after ICU care was completed and hospitalization after definitive management of pseudocyst.

### ERCP Findings

Each of the 53 patients who had been managed by delayed cholecystectomy who were found to have persistence of their pseudocyst had ERCP before definitive management. Similarly, all 49 of the patients in the early cholecystectomy group who had persistence of pseudocyst after cholecystec-

| TABLE 2. Percutaneous Drainage of Pseudocyst and Indications for That Intervention in Patients Treated With Early Cholecystectomy Compared With Patients Whose Pseudocyst Was Monitored and Cholecystectomy Was Delayed |
|--------------------------|-----------------|-----------------|-----------------|-----------------|
|                          | Referred from Outside Institution | Percutaneous Drain Placed | Infected as Indication for Drainage | Infected After Drain Placed |
| Patients assigned to undergo serial monitoring of fluid collections | 36/109 (33%) | 16/89* (18%) | 3/16* (19%) | 3/89* (3%) |
| Patients managed with early cholecystectomy | 41/78 (53%) | 31/62 (50%) | 16/31 (52%) | 13/31 (42%) |
| *P < 0.05 comparing serial monitoring with early cholecystectomy. |

| TABLE 3. Reoperation, Rehospitalization, and Postoperative Complications in Patients Managed With Early Cholecystectomy Compared With Patients Whose Pseudocysts Were Monitored and Cholecystectomy Delayed Until Resolution of Cyst or Persistence of Cyst |
|--------------------------|-----------------|-----------------|-----------------|
|                          | Reoperation After Cholecystectomy | Rehospitalization After Index Admission | Postoperative Complications |
| Patients assigned to undergo serial monitoring of fluid collection | 0/109* | 109/109 | 6/109* (5%) |
| Patients managed with early cholecystectomy | 49/78 (63%) | 49/78 (63%) | 34/78 (44%) |
| *P < 0.05 comparing serial monitoring to early cholecystectomy. |
tomy had ERCP performed before definitive care. By performing these ERCPs, we made an effort to correlate the persistence of cyst with pancreatic ductal changes based on a system that we have previously described (Fig. 1). Failure of the cyst to resolve appeared to correlate well with ductal anatomy. Of the 53 patients treated with delayed cholecystectomy, none had type 1 changes in their pancreatic duct as seen by ERCP, 9 patients had type 2 changes, 19 had type 3 changes, 9 had type 4 changes, and 16 had type 5 changes. None of the patients had chronic pancreatitis; thus none of them had type 6 or type 7 changes. Among the 49 patients treated with early cholecystectomy who had persistence of pseudocyst 6 patients had type 1 changes. Seven of these patients had type 2 changes in their pancreatic duct. An additional 7 had type 3 changes, 24 had type 4 changes, and 5 had type 5 changes. Each of these ductal abnormalities appeared to correlate with the persistence of pseudocyst.

Table 5 delineates the changes in the pancreatic duct seen in each of the 2 categories of patients: those with early operation and those with delayed operation.

**DISCUSSION**

Most of the literature which exists regarding moderate to severe acute pancreatitis has focused upon the critical care aspects of these patients. Considerable information is known regarding the recognition of necrosis of the pancreas in early evaluation of these patients and about distinguishing sterile versus infected necrosis. Studies have confirmed that there is no difference between gallstone-induced acute pancreatitis and other forms of acute pancreatitis. It is certainly well recognized that cholecystectomy is necessary after an episode of acute biliary pancreatitis and that delay in cholecystectomy raises the risk of recurrence of pancreatitis. It is an established practice that patients admitted for a mild initial acute pancreatitis caused by gallstones have their cholecystectomy performed after resolution of the clinical picture of acute pancreatitis. The urgency for this intervention assumes less significance in the presence of moderate to severe acute pancreatitis.
pancreatitis in which management of the pancreatitis dominates the clinical picture. There are some patients whose pancreatitis is so severe that they simply do not survive to their cholecystectomy and others whose cholecystectomy is performed during an exploration for necrosectomy. We are unaware of any data regarding the incidence of intercurrent episodes of acute pancreatitis during this phase of management of severe acute pancreatitis in a critical care setting. Such an event is not reported in large series of patients with this diagnosis.

Using severity-grading systems as a means of segregating those patients who are at the highest risk for morbidity and death from acute pancreatitis is well established. None of these systems include specific attention to the formation of peripancreatic fluid collections as a contributor to outcome. Balthazar has identified an important correlation between moderate and severe acute pancreatitis and the formation of fluid collections. The fact that a peripancreatic fluid collection and specifically pseudocyst must be considered in the timing of cholecystectomy after an episode of moderate to severe gallstone-induced pancreatitis has not been addressed previously in the literature by our searches. Certainly there are ample reports in the literature regarding the timing of intervention for pseudocyst. Although the data have varied, the general consensus has been that a 6-week interval after identifying a pseudocyst is reasonable for monitoring a pseudocyst. Improvements in imaging have greatly assisted in determining cyst wall maturity; to a degree, one may argue that the 6-week mandatory wait is no longer necessary to establish the maturity of the cyst wall. Most of us still operate under the edict first reported by Bradley et al in 1979 that complications related to pseudocysts appear to rise significantly in frequency in a pseudocyst that persists beyond 6 weeks. In our view, there thus arises a conflict in 2 standard precepts in pancreatic surgery. The first of these is that early cholecystectomy is required in patients who have had gallstone pancreatitis. Opposed to this strategy is the fact that peripancreatic fluid collections and pseudocysts should be evaluated for approximately 6 weeks to establish whether they are able to resolve and to assess the appropriateness of interventions. It is the purpose of this report to provide some clarity to this apparent puzzle.

A consequence of this lack of clarity is the common sequence of events in our practice in which a patient is referred for evaluation of a pseudocyst, infected or symptomatic, who has had moderate to severe acute biliary pancreatitis and prompt cholecystectomy. Concomitant use of percutaneous or endoscopic management of the cyst is commonly seen. The fact that these patients have already undergone a general anesthetic and an operative procedure and subsequently require a second interventional procedure and often a second operative procedure with another general anesthetic suggests to us that a clear strategy does not exist in the literature for the best management of such patients. Several reports have assessed the safety of early cholecystectomy. Uhl and Buchler have determined that cholecystectomy after an episode of severe pancreatitis should be delayed at least 3 weeks because of the risk of infectious complications, which were unacceptably high in patients who had cholecystectomy more promptly after their attack of pancreatitis. These data support our policy; however, little attention was given to the role played by fluid collections in these patients. Our data support the assertion that early cholecystectomy may raise the risk of infected pseudocyst. Percutaneous drainage fails in as many as 40% of patients so treated. We have previously reviewed the success rates for the percutaneous drainage of pseudocysts and have compared these to operative drainage. We have also reviewed the pancreatic ductal anatomy as a means of predicting those patients who are best suited to percutaneous drainage and who are least likely to have persistence of drainage and failure of percutaneous drainage. Ductal injuries were common in patients whose pseudocyst failed percutaneous drainage.

In the current study we have evaluated the safety of a policy of delayed cholecystectomy and observation in patients with peripancreatic fluid collection associated with gallstone-induced pancreatitis. Perhaps most surprising but encouraging was the fact that no patient in the delayed

### TABLE 5. Categories of Main Pancreatic Ductal Anatomy From ERCP Evaluation of Patients With Persistent Pseudocyst After Minimum 42 Days Monitoring in Patients Treated With Early Cholecystectomy Compared With Patients Having Delayed Cholecystectomy

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cholecystectomy groups sustained another episode of acute pancreatitis during our monitoring. Although our mean length of monitoring is not excessive, these data differ somewhat from the conventional belief that a recurrent episode of acute pancreatitis may be anticipated in fewer than 6 weeks after the initial episode of gallstone-induced pancreatitis. We can only speculate why our data diverge from these. It is conceivable that the severity of the attack of acute pancreatitis imparts some form of protection or perhaps creates a pattern that differs from patterns seen with simple edematous acute pancreatitis induced by gallstones. As stated previously, it is interesting that evaluations of severe acute pancreatitis make little mention of recurrent episodes of gallstone-induced pancreatitis during their management. Our data suggests that delayed cholecystectomy is safe in this group of patients.

The fact that each of the patients managed by a delayed cholecystectomy and monitoring required only 1 operative procedure itself establishes a major advantage for our policy compared with the 49 of 62 early cholecystectomy patients with fluid collections who required 2 operative procedures. Fully half of the patients who underwent early cholecystectomy who had fluid collections documented after their episode of moderate to severe acute pancreatitis had percutaneous drainage. Only 18% of patients managed with delayed cholecystectomy required this modality. The frequency of infected pseudocyst was also far more common in the early cholecystectomy patients. We can only speculate that the reason for this disparity is that cholecystectomy raises the risk of contamination and of subsequent infected pseudocyst. The fact that percutaneous drainage causes infected pseudocyst is an alternative explanation. We thus state that our data confirm that early cholecystectomy without addressing peripancreatic fluid collections is both ill-advised because of the possible need for a second general anesthesia and also potentially hazardous with a risk of converting stable fluid collection to an infected fluid collection and an urgent or emergent condition.

A significant flaw in our study is the fact that the actual number of patients managed by early cholecystectomy is not known, particularly in those patients who were transferred into our facility. It is certainly conceivable that many patients had favorable outcomes after early cholecystectomy. The increased frequency of infection is likely a reliable observation, but it may be elevated partly because of selection bias inherent in our method of patient inclusion. Spontaneous resolution of pseudocyst was twice as common in our delayed cholecystectomy patients. Some early cholecystectomy patients who had spontaneous resolution of their pseudocysts would have no need to seek our care and therefore are not represented in our data.

We have used percutaneous drainage in our delayed cholecystectomy group. Our most common indication was not infected fluid collection, although 6 of our patients treated with percutaneous drainage did have infected fluid collections before drainage. Percutaneous drainage was used in our monitored group in 10 patients because their status was essentially stable, but they were nutritionally unsound and considered to be at significant risk for operation in their current status. We used percutaneous drainage as a bridge between the initial management and the definitive operative procedure. This intervention was more often used to facilitate nutritional intake and to permit the patient to be discharged to home eating while awaiting final resolution of the cyst. In patients managed in this fashion, the persistence of pseudocyst was actually a persistent pancreatic fistula from the percutaneous drainage. We continue to believe that this is an appropriate application of percutaneous drainage and would advocate its use in such patients to ensure a safe operation. We acknowledge the fact that the indications for percutaneous drainage at outside institutions and even within our own institution by other practitioners may vary widely and thus may skew raw data inappropriately and make definitive conclusions regarding percutaneous drainage unreachable.

Endoscopic transpapillary stent drainage was developed relatively more recently. Our review of this literature suggests that pancreatic ductal stents have often been placed long before spontaneous resolution could take place. The significant concern raised by our study is the possibility that transpapillary drainage actually serves to contaminate the pseudocyst. Our total numbers are too small to draw conclusions, but the fact that 9 of 13 patients in our early cholecystectomy group who had transpapillary stents placed had episodes of sepsis is a concern. It is important to recognize this added risk of transpapillary drainage.

Our prior studies looking at pancreatic ductal anatomy in relation to pseudocyst behavior seem to be supported by the data generated in this study.15,16 We perform ERCP as a routine in patients with pseudocyst who are about to undergo an intervention. This is applied both for patients about to undergo a percutaneous drainage as well as for those who are treated with operative decompression. Our data for patients with early cholecystectomy and those with delayed cholecystectomy strongly suggest that pancreatic ductal abnormalities play a role in the persistence of pseudocyst over time. We are not prepared to suggest that this fact warrants an earlier ERCP. At some point and possibly using MRCP, we may identify ductal anatomy that predicts persistence of pseudocyst. Since we do not have information regarding ductal anatomy in patients who had spontaneous resolution of cysts, we cannot assume that ductal abnormalities will always result in persistence of cysts.

Patients who were managed with simple laparoscopic cholecystectomy after spontaneous resolution of their pseudocyst in the delayed cholecystectomy group had no complications and very short repeat hospitalization. Complications and length of hospitalization after operative pseudocyst drainage is comparable in the early and delayed chole-
cystectomy groups. Our data suggest that the length of initial hospitalization is comparable between the 2 groups but that the length of hospitalization after cholecystectomy is considerably shorter in the delayed cholecystectomy group and the number of rehospitalizations is considerably higher in the patients who underwent early cholecystectomy. All of these facts provide additional support for our policy of monitoring fluid collections and delaying cholecystectomy until the fluid collections have either resolved or have been determined to be persistent and therefore require intervention.

We acknowledge the fact that we have philosophically leaned toward performing a simultaneous operative management of the pseudocyst in patients who we know will require general anesthetic for their cholecystectomy. The basis for this position has been the fact that general anesthetic is already required and that the success rates for operative drainage of pseudocysts greatly exceed the success rates for either interventional radiologic or for endoscopic management.9–13 Having said this, we must concede that nonoperative management of the pseudocyst in our policy of delayed cholecystectomy may in fact be applicable in some patients. Our concern, particularly as we review the ductal anatomy in these patients leads us to believe that percutaneous drainage would have a higher failure rate in this subset of patients with significant ductal anatomic abnormalities based on our prior studies.15 We may infer from our data that moderate to severe acute pancreatitis is more likely associated with significant ductal injuries than simple acute pancreatitis with pseudocyst formation. Although we feel that our data are insufficient to prove that operative drainage of pseudocyst is the ideal management principle in patients managed by our policy of delayed cholecystectomy, we feel still that this represents the best management principle for the permanent resolution of these lesions. Attention to the existence of fluid collections in patients with moderate to severe acute biliary pancreatitis is mandatory in designing appropriate strategies.

REFERENCES


Discussions

DR. HENRY A. PITT (MILWAUKEE, WISCONSIN): I would like to thank the authors for providing the manuscript well in advance, and I congratulate them on their analysis of a large number of patients with severe gallstone pancreatitis, 80% of whom had fluid collections. Two thirds of these patients came to cystenterostomy. This retrospective analysis suggests that patients managed expectantly had fewer complications and a shorter overall hospital stay than patients managed with early cholecystectomy. These observations are important, and I personally agree with the authors’ conclusions that expectant management is preferred. Obviously, the data from a prospective randomized study would be better; however, with so many specialists and treatment options available for these patients, randomized studies of pseudocyst management have been difficult to perform. To further clarify the authors’ presentation, I have 3 questions.

My first basic question is whether the early cholecystectomy and the expectant management groups were comparable? All patients included in this analysis had more than 5 of Ranson’s signs. However, was the mean number of Ranson’s signs in the 2 groups comparable? In addition, were the 2 groups similar with respect to age, gender, CT scan findings, and associated diseases such as obesity, diabetes, and renal disease, which may have affected outcome?

My second question relates to the use of early endoscopic sphincterotomy and stone extraction in these patients. In patients with severe gallstone pancreatitis, prospective randomized trials have consistently demonstrated that patients undergoing early endoscopic sphincterotomy do better
than those undergoing early surgery. How many patients in each group underwent early endoscopic sphincterotomy? If this management did differ between the 2 groups, do you believe that this part of their management may have affected the ultimate outcome of the patients?

My final question relates to the use of parenteral and enteral nutrition in these patients. As you know, when TPN is used, septic complications are increased. Was the use of TPN comparable in the 2 groups?

DR. KEVIN E. BEHRNS (CHAPEL HILL, NORTH CAROLINA): Thank you, Dr. Nealon, for an excellent presentation and for providing me with a copy of the manuscript. Congratulations on investigating a topic that has not been adequately addressed despite multiple studies that have examined the timing of cholecystectomy in gallstone-induced acute pancreatitis.

The question of the optimal time for cholecystectomy in patients with moderate to severe acute pancreatitis associated with peripancreatic fluid collections or pseudocysts has not been investigated directly. This study incorporates findings of a large group of patients who have pseudocysts complicated by fluid collections with the need to perform a cholecystectomy.

Your findings strongly suggest that patients who undergo delayed cholecystectomy do markedly better than those who have early cholecystectomy in terms of sepsis, morbidity, reoperation, and repeat hospital admission rates and hospital length of stay. Therefore, on the basis of your data, you correctly advocate for delayed cholecystectomy.

But concomitant with cholecystectomy you also recommend operative management of residual pancreatic pseudocysts. Although your data provide a strong case for delayed cholecystectomy, it appears that the number of patients who require concomitant pseudocystic drainage is relatively high. This may be due to the policy of operating on patients who had not resolved pseudocysts by 6 weeks.

What was the mean time to operation in the 53 patients who had cholecystectomy combined with pseudocyst drainage? Perhaps a short time period was not of sufficient duration to prevent pseudocyst resolution. Also, what was the size of the pseudocysts and how many of these patients with pseudocysts were symptomatic?

Finally, related to Dr. Pitt’s question, since all patients had an ERCP and what we are truly trying to prevent is recurrent gallstone-induced pancreatitis, why not do an endoscopic sphincterotomy at the time of the ERCP? This would decrease the risk of recurrent pancreatitis and allow more time for pseudocyst resolution, potentially decreasing the number of patients requiring operative intervention for a pseudocyst? We have done this on a few select patients with no adverse outcome.

This is a timely study. And I thank Dr. Nealon for allowing me to review the paper and the Association for the privilege of discussing it.

DR. STEVEN C. STAIN (NASHVILLE, TENNESSEE): I have 2 questions. First, regarding the percutaneously drained group, from my understanding there were 6 patients in the monitored group and 29 in the early operation group who had percutaneous drainage. What was the success rate of those who were drained, and was a positive culture in either group an indication for operation? If that was the case, that may explain the higher incidence of reoperation in patients in the early operative group.

My second question relates to the endoscopic transpapillary stent drainage group. Nine of the 13 patients who had endoscopic drainage had sepsis. Should we conclude that no patient should be treated with endoscopic drainage if they have moderately severe pancreatitis?

DR. WILLIAM H. NEALON (GALVESTON, TEXAS): The question of how comparable these 2 populations are is key. Since many of the early cholecystectomy patients came from outside institutions, we don’t know the denominator of that group, and there may well be many who had early cholecystectomy without incident. That fact is going to certainly affect how comparable these 2 groups can be. I still believe that the phenomenon is frequent enough, and I have to guess there are many in the audience who have these kinds of patients transferred into their care often in a year. We did not find differences in the mean number of Ranson signs, the sizes of the pseudocysts, the presence of obesity, renal failure, age, etc. None of these turned out to establish clear differences in the 2 groups.

Early ERCP and stone extraction is certainly an option in the literature for very severe acute biliary pancreatitis. We have used that in 3 of our patients in the monitored group and 4 of the patients in the early cholecystectomy group. These are intended more as a rescue type of a procedure early in the course of disease. I do not advocate ERCP early in the management of severe acute pancreatitis otherwise. There certainly exists a significant risk in our opinion for infecting the pseudocyst fluid collection at the time of that procedure.

We did not specifically extract TPN as a risk factor, although I must say that a considerable percentage of the patients transferred to our institution from outside come without TPN. Many of those who have had prolonged ICU stays have been on TPN, although we have not specifically looked at that as a separate measure.

Dr. Behrns, I thank you for your comments and suggestions. Our mean time of delay before the cyst-enterostomy is slightly longer than the 7 weeks in our policy. This was influenced by the intensive care stay. Our mean stay in those patients who had cholecystectomy combined with pseudocyst drainage is slightly longer than the 7 weeks in our policy.
who have ended up requiring a drainage procedure was on the order of 9 weeks.

The size of the pseudocyst that we finally drained was always greater than 5 cm. However, we have a subset of those who have had a percutaneous drain where we literally have a collapsed pseudocyst with a persistent fistula, so assessing size in those patients is not possible. We found symptoms in 92% of these patients, so we think symptoms are quite common.

We do perform ERCP. And I didn’t mention in my presentation but I mention in the paper that we made a correlation with pancreatic ductal abnormalities in these patients who have persistent cysts. I am guessing in your question you are referring to the fact that there can be a choice of percutaneous, endoscopic, or operative management of cysts. I will admit that it is my philosophy that since operative drainage of pseudocysts has a success rate of 98% to 99% whereas percutaneous and endoscopic in my review of the literature has a success rate of about 65 to 70%. I believe the fact that you are already going to do a general anesthetic may lead one to preferentially proceed with intraoperative drainage of the pseudocyst at the time.

Dr. Stain, thank you for your comments. Six of the monitored group and 31 of the early operation group had percutaneous drainage. Six of those were successful long-term in managing the pseudocysts with resolution. Transpapillary stents worry me. I would say if you have a cyst with solid matter in it one should be aware that we are actually establishing a connection between contaminated gut and the cyst when you perform a transpapillary stent. For all nonoperative management of pseudocyst, one must remain vigilant regarding possible contamination and sepsis occurring in a previously sterile cyst.