World J. Surg. 27, 256–259, 2003
DOI: 10.1007/s00268-002-6647-3

WORLD
Journal of
SURGERY

Timing of Cholecystectomy for Acute Biliary Pancreatitis: Outcomes of Cholecystectomy on First Admission and after Recurrent Biliary Pancreatitis

Orhan Alimoglu, M.D., Orhan V. Ozkan, M.D., Mustafa Sahin, M.D., Adem Akcakaya, M.D., Ramazan Eryilmaz, M.D., Gurhan Bas, M.D.

First Department of Surgery, Vakif Gureba Training Hospital, 34280 Çapa, Istanbul, Turkey

Abstract. Biliary stones are the leading cause of acute pancreatitis. Although cholecystectomy and selective endoscopic retrograde cholangiography (ERC) comprise the current treatment in patients with acute biliary pancreatitis (ABP), the time of intervention is still controversial. In this study we evaluated the outcomes of cholecystectomy on first admission for ABP and in patients with recurrent biliary pancreatitis. A series of 43 patients with ABP between January 1997 and November 2000 were evaluated retrospectively. Patients were classified into two groups. Group I included 27 patients who underwent cholecystectomy on first admission before discharge from the hospital. Group II comprised 16 patients who had recurrent biliary pancreatitis and then underwent cholecystectomy. The severity of the pancreatitis was determined by Ranson's criteria. Age, gender, length of hospital stay, severity of pancreatitis, amylase level, and complications of cholecystectomy were evaluated in both groups. Patients in group I underwent cholecystectomy during the original hospital admission and patients in group II during an admission for a recurrence. There were 24 patients with a Ranson's score ≤ 3 in group I and 12 in group II. The mean hospital stays were 15.29 days (range 4–48 days) and 36.66 days (range 15–123 days) in groups I and II, respectively ($p = 0.006$). Morbidity was 11% without mortality in group I and 43% with one mortality in group II ($p = 0.023$). Definitive treatment of ABP can be accomplished effectively and safely by cholecystectomy following clinical improvement, with selective ERC performed during the first admission (delayed cholecystectomy). Waiting to perform cholecystectomy (interval cholecystectomy) may result in recurrent biliary pancreatitis, which may increase morbidity and the length of the hospital stay.

Biliary calculi (stone, microlithiasis, sludge) are the leading cause of acute pancreatitis (AP). The relation between a biliary calculus and acute biliary pancreatitis (ABP) was first proposed by Opie in 1901 [1] and was confirmed by Acosta and Ledsesma [2] and Kelly [3].

The pathogenesis of ABP involves a temporary obstruction of the ampulla of Vater by a biliary calculus migrating from the bile duct to the duodenum, causing bile reflux into the pancreas via a common channel; or when a stone is passed, the sphincter is "opened" temporarily, allowing regurgitation from the duodenum back up into the pancreatic duct [1, 2, 4, 5]. Both cause AP. Evidence for this pathogenesis includes recovering stones from the stool in 86% [6] of patients with ABP and detecting stone impaction in the ampulla of Vater in 72% [7] of patients who underwent emergent surgery.

For this etiology, although clearance of the common bile duct (CBD) and gallbladder removal were generally accepted, proper timing of the intervention was controversial before the endoscopic and laparoscopic era; and the controversy is ongoing. After the advent of endoscopic retrograde cholangiography (ERC) and endoscopic sphincterotomy (ES) for clearing the CBD, early surgery (within 24–48 hours of admission) has lost some of its importance.

For cholecystectomy there are two approaches that concern proper timing: (1) interval cholecystectomy: postponing cholecystectomy 6 to 8 weeks may reduce the acute inflammation, making it easier to perform laparoscopic cholecystectomy (LC) and possibly lowering the conversion rate [8]; (2) delayed cholecystectomy (48 hours after admission): performing cholecystectomy during the first admission after clinical improvement may reduce the incidence of recurrent attacks of ABP, morbidity, and hospital expenses [9]. In this study, we evaluated the outcomes of cholecystectomy during the first admission (delayed surgery) for ABP and in recurrent biliary pancreatitis patients who underwent interval surgery after the first attack.

Materials and Methods

Patients

A total of 43 patients with the diagnosis of ABP were evaluated retrospectively at the 1st Department of Surgery, Vakif Gureba Training Hospital (Istanbul) from January 1997 to November 2000. The diagnosis was based on the presence of the following: (1) acute abdominal pain and tenderness; (2) elevated serum amylase level of more than 1000 IU/L; (3) biliary calculus in the biliary tree detected by ultrasonography (US); and (4) no history of alcoholism,

This International Society of Surgery/Société Internationale de Chirurgie (ISS/SIC) article was presented at the 39th World Congress of Surgery International Surgical Week (ISW01), Brussels, Belgium, August 26-30, 2001.

Correspondence to: Orhan Alimoglu, M.D., Kazimkarabekir Mah. Hekim Suyu Cad., Dostluk Sitesi D 1 Blok D:13 34080 Kucukkoy, GOP, Istanbul, Turkey, e-mail: oalimoglu@yahoo.com

hypercalcemia, or lipid disorders [9]. Abdominal US was performed within 24 hours of admission. The severity of the disease was determined by Ranson's prognostic signs [10, 11]: three or fewer signs indicated mild disease; more than three signs indicated severe disease.

Methods

After the diagnosis of ABP was established, the following medical treatment modalities were employed: (1) nothing was given by mouth; (2) intravenous fluids, electrolytes, and H_2-receptor blockers were administered; (3) nasogastric drainage was performed if patients had vomiting and nausea; (4) meperidine HCl for pain and antibiotics for fever were administered when needed.

Patients who met one or both of the following criteria underwent early ERC and, if indicated, ES: (1) elevated serum bilirubin, γ-glutamyl transferase, alkaline phosphatase, and aspartate aminotransferase (AST); and (2) CBD diameter > 7 mm or US diagnosis of a biliary calculus in the CBD. Clinical improvement was determined by the serum amylase level returning to normal and alleviation of abdominal pain.

The only criterion for deciding whether patients underwent delayed or interval cholecystectomy was the surgeons' preference. Patients were evaluated in two groups. Group I comprised 27 patients who underwent cholecystecyomy and early (within 72 hours) selective ERC and ES on first admission before discharge from the hospital. Group II included 26 patients who underwent early selective ERC and ES during the first admission and were scheduled for interval cholecystectomy after their symptoms disappeared; 16 of these patients developed recurrent biliary pancreatitis and subsequently underwent early selective ERC/ES and cholecystectomy. Age, gender, length of hospital stay, severity of the pancreatitis, amylase level, and complications of cholecystectomy were evaluated in the two groups.

Statistical Analysis

Student's *t*-test, Fisher's exact test, and chi-square analysis were performed to analyze the data for significance between the groups. Mean values (SD) were calculated. Statistical significance was defined as $p < 0.05$.

Results

There were 27 patients (21 women, 6 men; mean age 54 years) in group I. Of the 26 patients who underwent interval cholecystectomy, 16 (8 women, 8 men; mean age 57 years) who had recurrent acute pancreatitis were included in group II. Of the 16 patients with recurrent pancreatitis, 9 had one, 5 had two, and 2 patients had three recurrent ABP attacks. The recurrence rate was 61%. The groups were matched for age and gender.

The mean amylase level on admission was 2676 U/L (range 1133–5933 U/L) in group I and 3961 U/L (range 1060–8345 U/L) in group II. Amylase levels returned to normal in 4.48 days (range 2–10 days) in group I and 3.93 days (range 2–6 days) in group II. Biochemical analyses are shown in Table 1. Altogether, 24 patients in group I had a Ranson's score of 3 or less, as did 12 in group II ($p = 0.39$).

Table 1. Results of biochemical analyses.

Biochemical parameters	Group I	Group II	Normal values
AST	270.0 ± 213.84	179.0 ± 164.94	0–38 U/L
Alkaline phosphatase	320.0 ± 211.85	291.0 ± 172.14	39–117 U/L
GGT	276.0 ± 287.08	284.0 ± 325.60	7–49 U/L
LDH	617.0 ± 294.81	653.0 ± 432.86	240–480 U/L
Total bilirubin	3.15 ± 3.44	1.94 ± 1.22	0–1.20 mg/dl
Direct bilirubin	2.19 ± 2.92	1.12 ± 1.00	0–0.95 mg/dl

AST: aspartate aminotransferase; GGT: γ-glutamyltransferase; LDH: lactate dehydrogenase.

Table 2. Patient complaints.

Complaint	Group I (no.) ($n = 27$)	Group II (no.) ($n = 16$)
Abdominal pain	27 (100%)	16 (100%)
Nausea	20 (74.1%)	11 (68.8%)
Vomiting	15 (55.6%)	10 (62.5%)
Jaundice	5 (18.5%)	3 (18.8%)

Table 3. Complications of cholecystectomy.

Complication	Group I (no.)	Group II (no.)
Lung infection	2	3
Myocardial infarction	—	1
Wound infection	1	3
Total	3	7

The most common complaint of the patients on admission was abdominal pain. The patients' complaints are shown in Table 2.

Early selective ERC was performed in 19 patients (70% of cases) in group I (with one failure) and 12 patients (4 during the first admission and 8 during the recurrence) (75% of cases) in group II. Ductal stones, microlithiasis, and sludge were demonstrated in 14 patients in group I and in 8 patients in group II. All these patients underwent ES and removal of biliary calculous endoscopically.

There were three complications of sphincterotomy in group I. One hemorrhage occurred and was managed by transfusion. Two complications occurred in group II: Pancreatitis in one patient was managed with conservative treatment, and one retroperitoneal abscess due to perforation was managed with percutaneous drainage. Both groups were matched for therapeutic ERC and its complications.

Laparoscopic cholecystectomy was performed in 25 patients in group I and in 14 patients in group II, with one conversion in each group. Morbidity after surgery was significantly higher in group II than group I: 43% and 11%, respectively ($p = 0.023$). The complications of cholecystectomy are shown in Table 3.

Two patients in group II and one in group I had severe pancreatitis and underwent laparotomy for necrotizing pancreatitis and cholecystectomy. One patient in group I had a pseudocyst and underwent percutaneous drainage and open cholecystectomy. One patient in group II with severe disease died owing to multiorgan failure.

The mean hospital stay was significantly longer in group II than in group I: 36.66 days (range 15–123 days) and 15.29 days (range 4–48 days), respectively ($p = 0.006$). The mean number of admisions was 2.56 for the interval cholecystectomy group.

Discussion

Treatment of ABP is challenging, and proper timing of any intervention is the most important factor for solving this clinical dilemma. Although procedures are similar, there are three approaches to appropriate timing of ERC and cholecystectomy (early, delayed, and interval).

Before the advent of endoscopy, early and delayed surgery had been discussed for years. Whereas some advocated early surgery for urgent biliary decompression and removal of an impacted stone from the ampulla of Vater to prevent progression of the disease [7, 12], others advocated delayed surgery, believing that the course of gallstone pancreatitis is not improved by early stone removal and that an impacted stone can pass into the duodenum without intervention [6, 9, 13].

After the advent of ERC, the importance of early surgery has diminished, as an impacted stone can be removed and biliary decompression performed by ERC and ES. With the advent of ERC, new controversies have emerged regarding when and in whom these procedures should be performed.

It has been recommended that ERC be performed early in patients with severe biliary pancreatitis and in whom the disease worsened or in patients with cholangitis and jaundice [14]. It was shown that early ERC and ES can reduce morbidity and mortality in patients with severe ABP [15, 16]. On the other hand, it was shown that performing ERC in all patients with ABP is unnecessary and cost-ineffective [17, 18].

We performed early elective ERC in 19 patients in group I (with one failure) and in 12 patients in group II who were strongly suspected to have CBD stones based on biochemical parameters and US findings. CBD calculi were detected in 14 patients (77%) in group I and 8 patients (66%) in group II. The overall morbidity associated with the endoscopic procedure was 9%, and there were no deaths.

Although the results of ERC and ES in the study correlated with those in the literature, five patients (26% of patients who underwent ERC and ES) in group I and four patients (33% of those who underwent ERC and ES) in group II underwent unnecessary ERC and ES, including most recent cases of this study. When the presence of a bile duct stone is strongly suspected, we prefer magnetic resonance imaging (MRI) cholangiography to avoid unnecessary ERC and are now using ERC for therapeutic purposes.

With the advent of laparoscopy and endoscopy, although early cholecystectomy is not recommended, timing of cholecystectomy following ABP is controversial. There are two approaches concerning proper timing of cholecystectomy: delayed and interval cholecystectomy. Initially, LC was not suggested in patients with ABP [19], but later it was concluded that LC is the preferred treatment with an increased rate of conversion [8]. Today, although some believe that LC can be performed safely and effectively as a delayed approach, except for severe ABP [20, 21], others advocate interval LC following ERC [22]. It is thought that the interval may allow the inflammatory process to settle, but it has been shown that postponing LC is not advantageous surgically and cannot alleviate severe adhesions or avoid difficult dissection of the gallbladder, bleeding, or a prolonged operating time [23].

In this study, we performed delayed LC in 25 (92%) patients in group I and 14 (82%) patients in group II, with one conversion in each group. We believe that delayed LC can be performed safely in patients with ABP.

Interval cholecystectomy reportedly causes recurrent pancreatitis in 30% to 50% [20]; we observed a 61% recurrence rate in our study. Furthermore, five patients had two recurrent attacks, and two patients had three. We believe that recurrent attacks cannot be prevented unless cholecystectomy is performed during the first admission.

The interval procedure also increased the length of hospital stay and caused morbidity among our cases. The mean hospital stay was 36.66 days in the interval cholecystectomy group and 15.29 days in the delayed cholecystectomy group. Morbidity after surgery was 43% in the interval group and 11% in the delayed group.

One patient in group I and two patients in group II had necrotizing pancreatitis and underwent laparotomy. ERC was performed in these patients before laparotomy. One of the patients in the interval group (6.2%) died of multiorgan failure; there were no deaths in the delayed group.

Conclusions

Although it was recommended during the early 1980s to perform cholecystectomy during the first admission in patients with ABP, a retrospective review of our records revealed that 49% of our patients underwent interval cholecystectomy. Interval cholecystectomy may result in recurrent biliary pancreatitis, which may increase morbidity and the hospital stay. Cholecystectomy should be performed during the first admission after clinical improvement with early selective ERC in patients with ABP.

Résumé. La lithiase biliaire est la première cause de pancréatite aiguë. Bien que la cholécystectomie et la CPRE sélective soient admises par tout le monde comme le traitement actuel des patients atteints de pancréatite aiguë biliaire (PAB), le meilleur moment pour intervenir est toujours discuté. Dans cette étude, nous avons évalué l'évolution des cholécystectomies pratiquées lors de la première admission pour PAB et pour pancréatite biliaire récidivante. Entre jan 1997 et nov 2000, 43 patients atteints de PAB ont été évalués rétrospectivement. Les patients ont été classés en deux groupes. Dans le groupe I, il y avait 27 patients qui ont eu une cholécystectomie lors de leur première admission au cours de la même hospitalisation. Dans le groupe II, on a dénombré 16 patients qui ont eu leur cholécystectomie lors de la pancréatite récidivante. La sévérité de la pancréatite a été déterminée par le score de Ranson. L'âge, le sexe, la durée de l'hospitalisation, la sévérité de la pancréatite, le taux d'amylasémie et les complications de la cholécystectomie ont été évalués dans les deux groupes. Vingt-quatre patients avaient un score de Ranson en-dessous de 3 dans le premier groupe et 12, dans le deuxième groupe. La durée moyenne du séjour hospitalier a été de 15.29 jours (extrêmes 4 à 48) et de 36.66 jours (extrêmes 15 à 123) dans les groupes I et II, respectivement ($p = 0.006$). La morbidité a été de 11% sans mortalité et de 43% avec un décès dans les groupes I et II, respectivement ($p = 0.023$). Après amélioration clinique, le traitement définitif de la PAB peut être réalisé efficacement et avec sûreté par cholécystectomie et CPRE sélective lors de la première hospitalisation. Retarder la cholécystectomie peut se solder par une pancréatite biliaire récidivante et ceci peut augmenter la morbidité et la durée de l'hospitalisation.

Resumen. Los cálculos biliares son la principal causa de pancreatitis aguda. Aunque actualmente la colecistectomía con CER es el tratamiento de preferencia en la pancreatitis biliar aguda (PBA), sigue siendo motivo de controversia el momento en que se debe realizar la intervención. En el presente estudio hemos evaluado el resultado de la colecistectomía en la PBA practicada durante la primera admisión y en la pancreatitis biliar recurrente; 43 pacientes atendidos entre enero de 1997 y noviembre de 2000 fueron analizados en forma retrospectiva, clasificándolos en dos grupos: grupo I, 27 pacientes sometidos a colecistectomía practicada durante la primera admisión, y grupo II, 16 pacientes que presentaron pancreatitis recurrente y que fueron sometidos a colecistectomía. La gravedad de la pancreatitis fue determinada por los criterios de Ranson. Se hizo el análisis de la edad, la duración de la hospitalización, la gravedad de la

pancreatitis, la concentración de la amilasa sérica y las complicaciones de la colecistectomía en ambos grupos. Los pacientes del grupo I fueron sometidos a colecistectomía en el curso de su hospitalización primaria, y los del grupo II con ocasión de la recurrencia. Veinticuatro pacientes exhibieron un puntaje de Ranson menor de 3 en el grupo I y 12 en el grupo II. La duración de la hospitalización fue 15.29 días (rango 4–48) y 36.6 días (rango 15–23) en los grupos I y II, respectivamente ($p = 0.006$). La tasa de morbilidad fue 11% y cero mortalidad en el grupo I y 43% y una muerte en el grupo II ($p = 0.023$). Nuestra conclusión es que el tratamiento definitivo de la PBA puede ser realizado en forma segura una vez haya mejoría clínica, mediante colecistectomía con CER selectiva practicada durante la hospitalización inicial. La colecistectomía de intervalo puede dar lugar a pancreatitis recurrente, y ello puede aumentar la morbilidad y prolongar la hospitalización.

References

1. Opie EL. The etiology of acute hemorrhagic pancreatitis. Bull. Johns Hopkins Hosp. 1901;12:182–188
2. Acosta JM, Ledsesma CL. Gallstone migration as a cause of acute pancreatitis. N. Engl. J. Med. 1974;290:484–487
3. Kelly TR. Gallstone pancreatitis pathophysiology. Surgery 1976;80:488
4. Kelly TR, Swaney PE. Gallstone pancreatitis: the second time around. Surgery 1982;92:571–575
5. Acosta JM, Pellegrini CA, Skinner DB. Etiology and pathogenesis of acute biliary pancreatitis. Surgery 1980;88:118–125
6. Kelly TR. Gallstone pancreatitis: the timing of surgery. Surgery 1980; 88:345–350
7. Acosta JM, Rossi R, Galli OM, et al. Early surgery for acute gallstone pancreatitis: evaluation of a systematic approach. Surgery 1978;83:367–370
8. Tate JJ, Lau WY, Li AK. Laparoscopic cholecystectomy for biliary pancreatitis. Br. J. Surg. 1994;81:720–722
9. Kelly TR, Wagner DS. Gallstone pancreatitis: a prospective randomized trial of the timing of surgery. Surgery 1988;104:600–605
10. Ranson JH, Rifkind KM, Roses DF, et al. Prognostic signs and the role of operative management in acute pancreatitis. Surg. Gynecol. Obstet. 1974;139:69–81
11. Ranson JH. Etiological and prognostic factors in human acute pancreatitis: a review. Am. J. Gastroenterol. 1982;77:633–638
12. Stone HH, Fabian TC, Dunlop WE. Gallstone pancreatitis: biliary tract pathology in relation to time of operation. Ann. Surg. 1981;194:305–312
13. Ranson JH. The timing of biliary surgery in acute pancreatitis. Ann. Surg. 1979;189:654–663
14. Mergener K, Baillie J. Endoscopic treatment for acute biliary pancreatitis: when and in whom? Gastroenterol. Clin. North Am. 1999;28: 601–613
15. Neoptolemos JP, Carr-locke DL, London NJ, et al. Controlled trial of urgent endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy versus conservative treatment for acute pancreatitis due to gallstones. Lancet 1988;2:979–983
16. Fan ST, Lai EC, Mok FP, et al. Early treatment of acute biliary pancreatitis by endoscopic papillotomy. N. Engl. J. Med. 1993;328:228–232
17. Schwesinger WH, Page CP, Gross GW, et al. Biliary pancreatitis: the era of laparoscopic cholecystectomy. Arch. Surg. 1998;133:1103–1106
18. Baillie J. Treatment of acute biliary pancreatitis. N. Engl. J. Med. 1997; 336:286–287
19. Cuschieri A, Dubois F, Mouiel J, et al. The European experience with laparoscopic cholecystectomy. Am. J. Surg. 1991;161:385–387
20. Delorio AV Jr, Vitale GC, Reynolds M, et al. Acute biliary pancreatitis: the roles of laparoscopic cholecystectomy and endoscopic retrograde cholangiopancreatography. Surg. Endosc. 1995;9:392–396
21. Uhl W, Muller CA, Krahenbuhl L, et al. Acute gallstone pancreatitis: timing of laparoscopic cholecystectomy in mild and severe disease. Surg. Endosc. 1999;13:1070–1076
22. Liu CL, Lo CM, Fan ST. Acute biliary pancreatitis: diagnosis and management. World J. Surg. 1997;21:149–154
23. Schachter P, Peleg T, Cohen O. Interval laparoscopic cholecystectomy in the management of acute biliary pancreatitis. HPB Surg. 2000;11: 319–323