

Laparoscopic Cholecystectomy: Relationship of Pathology and Operative Time

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ABSTRACT

Objective: Controversy exists regarding the use and timing of laparoscopic cholecystectomy in the treatment of both acute and chronic cholecystitis. Acute advocates claim to avoid fibrosis and potential dissection injuries, whereas chronic proponents avoid poor visualization due to edema and possible conversion. This study of both acute and chronic cholecystitis cases examines the relationships between pathology, operative time, and outcome of laparoscopic cholecystectomy.

Methods: A retrospective review of medical records and pathology of acute (n = 9) and chronic (n = 62) laparoscopic cholecystectomy cases, performed by 2 surgeons from 1995 to 1999 was undertaken. Using multiple regression techniques, the relationship between operative time and age, sex, race, presenting symptoms, and degree of pathologic cholecystitis was evaluated.

Results: One case of acute gangrenous cholecystitis required conversion. None of the chronic cases required conversion. In single variable analysis, abnormal liver function tests, chronic inflammation, wall thickness, and number of stones were each predictive of longer operative time. However, in the multiple regression, abnormal liver function tests were the only clinical factor that remained a predictor of operative time (16 minutes longer, $P = 0.05$). Time from presentation to operation had no effect on operative time. Twelve patients had preoperative endoscopic retrograde cholangiopancreatography, and 4 had choledocholithiasis (acute n = 1, chronic n = 3). Two chronic patients required postoperative endoscopy for a cystic duct leak (n = 1) and choledocholithiasis (n = 1). The adjusted average operative

time for acute and chronic cases was similar (93 versus 74 minutes, $P > 0.05$).

Conclusion: Laparoscopic cholecystectomy can be done safely for both acute and chronic cholecystitis with similar operative times. Abnormal liver function tests are associated with longer operative time. Time lapse between presentation and operation has no effect on operative time or outcome.

Key Words: Laparoscopic cholecystectomy, Pathology, Operative time, Body mass index (BMI).

INTRODUCTION

Cholecystitis is a surgically managed disease that is most often treated by laparoscopic cholecystectomy. Cholecystectomy is necessary to avoid complications associated with the natural course of cholecystitis and its pathologic endpoints. Controversy exists regarding the use and timing of laparoscopic cholecystectomy for both acute and chronic cholecystitis. Technical difficulties can occur in the dissection of the gallbladder in both acute and chronic cases that can lead to poor results. Randomized studies¹ of open cholecystectomy done within 72 hours versus later surgery show no difference in bile duct injury rates. Proponents of early surgery avoid complications, such as fistula, and avoid the fibrosis that can lead to potential dissection injuries in chronic cases.^{2,3} Advocates of postponing surgery want to avoid the bleeding, edema, and conversion rates associated with more acute cholecystitis cases. Mixed results have been reported in the recent retrospective reviews of acute cholecystitis and laparoscopic cholecystectomy. Estes et al³ show a shorter length of stay, no need to convert, and no complications, whereas, Jatzko et al⁴ find acute cholecystitis associated with more complications. C. K. Kum et al⁵ note higher conversion rates and longer operative time for acute cases.

Pathologically, the spectrum of changes should be related to the operative outcome of laparoscopic cholecystectomy cases. In some reviews, discrepancy existed between the early "clinical" acute versus true "patholog-

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ically” acute cases. Indeed, only one third of clinical cases had pathology to support the diagnosis.³ The objective of this review is to examine and clarify the relationship between the pathology of cholecystitis and operative time and the outcome of laparoscopic cholecystectomy.

METHODS

A retrospective medical record review of laparoscopic cholecystectomy cases (acute n = 9, chronic n = 62) for 2 surgeons from 1995 to 1999 was undertaken. Variables examined included medical history, laboratory data, radiologic findings, treatment, operative time, pathology, and length of stay (**Table 1**). Time lapses over 1 year between diagnosis and operation were designated as maximal at 365 days. Body mass index (BMI) was calculated using a BMI calculator tool on the www.PHYS.com (2000 Conde’Net, Inc.) Internet Web site. Data required for this calculation included height, weight, age, and sex.

Each case of cholecystitis was reviewed by the pathologist and designated as either acute or chronic. Pathology was classified according to wall thickness, amount of fibrosis, muscle hypertrophy, inflammation, quantity of stones, and the presence of Rokitansky-Aschoff sinuses. These changes were graded on a scale of 0 to 4. Patients having subacute changes were categorized as acute. One acute case of gangrenous cholecystitis requiring conver-

sion was dropped from the main analysis. Patients with a history of pancreatitis, choledocholithiasis, and those requiring intraoperative cholangiograms were not excluded from the main analysis. The Student t test and Pearson chi-square test of proportions were used on certain demographic and pathologic data. Multiple linear regression was used to adjust for the above-mentioned variables, and their impact on operative times for the acute and chronic cases was examined.

RESULTS

Of the 2 surgeons included in this review, 1 had 20 years of hepatobiliary operative experience. The other had 5 years. Our patients’ racial distribution and average age were similar comparing chronic and acute cases, the majority of patients being under 65 years of age (**Table 2**). A predominance of men existed in the acute (67%) as compared with the chronic group (29%) (*P* = 0.026); however, overall more women patients (n = 47, 66%) existed.

Average parity for acute and chronic cases was two. Almost half of the cases had had prior abdominal surgery. These surgeries included cesarian delivery, appendectomy, ovarian cystectomy, tubal ligation, ectopic pregnancy, reversal of tubal ligation, colostomy, and umbilical hernia repair. The average body mass index

Table 1.
Variables Examined

Age	Pain
Amylase	Pancreatitis
Antibiotic treatment	Parity
Bile spill	Presence of fibrosis
Cholesterol	Presence of inflammation
Drain use	Presence of muscle hypertrophy
ERCP	Prior abdominal surgery
Fever	Quantity of stones
HIDA scan	Race
Length of stay	Rokitansky-Aschoff sinus
Leukocytosis	Sex
Liver function test (AST, ALT, ALK-Phos, Bilirubin)	Surgeon
Medical history	Time lapse between presentation and operation
Nausea/vomit	Ultrasound
Operative time Pain	Wall thickness

Table 2.
Demographics

	Acute	Chronic
Age		
Mean years	50 (Range 19-69)	47 (Range 23-77)
≥ 65 years	2	6
< 65 years	7	56
Sex (%male)	67*	29
Race (%)		
White	89	77
Black	11	13
Other	0	10
BMI (mean)	27.3	30.2
Diabetes (N)	0	11
Hyperlipidemia (N)	0	5
Parity (mean)	2	2(0-6)
Prior surgery (%)	50	49
Days to OR (mean days)	36 (Range 4-107)	83 (Range 4-365)
Leukocytosis (%)	71%	23%
Liver function elevation (%)	67	30
Amylase (mean)	40.8	201.8
Cholesterol (mean)	168.5	206.6
Antibiotic treatment (N)	7	23
Bile spill (N)	4	12
Drain (N)	2	1
Surgeon1 (%)	89	60
Surgeon2 (%)	11	40

*Pearson chi-square significant, $P = 0.02$

was also similar between acute and chronic cases. Most patients were obese, with a BMI over 25.

Patients were referred for cholelithiasis with varying symptom histories. Four patients had signs of gallstone pancreatitis [3 had (-) endoscopic retrograde cholangiopancreatography (ERCP)] and 4 others had ERCP-proven choledocholithiasis. Two patients had a history of hepatitis, 1 acute and 1 chronic. Patients presenting with the clinical triad of pain, leukocytosis, and fever included most acute cases and 3 chronic ones (2 of these had pancreatitis). All cases had pathologic changes consistent with acute or chronic cholecystitis. All of our diabetic patients (n = 11) were chronic cases, and all of the hyperlipidemia patients (n = 5) were chronic cases and were being treated medically.

Only 3 patients in this review underwent laparoscopic cholecystectomy within 10 days of presentation. Two of these had acute cholecystitis, and 1 required conversion. Time lapse from presentation to operation varied widely, most acute cases averaged a 5-week lag and chronic cases more than 11 weeks. This time period had no effect on operative time ($P = 0.3$). Pretreatment with antibiotics had no significant effect on operative time. The length of operation ranged between 30 and 150 minutes. The adjusted average operative time for acute and chronic cases was similar (93 vs. 74 minutes, $P > 0.05$, **Table 3**).

One third of patients in this review had elevated liver chemistries. Only 5 (5.6%) had ERCP-proven choledocholithiasis (**Table 4**). Three cases with elevated liver

Table 3.

Main Outcome: Operative Time

	Nonadjusted (min)	Adjusted (min)*
Acute [mean (range)]	94 (55-150)	93
Chronic [mean (range)]	72 (30-140)	74

*Adjusted for age, sex, race, liver function test, fever, stone quantity, wall size, chronic inflammation surgeon and BMI.

Table 4.

Elevated Liver Function Test

	Acute (n = 5)	Chronic (n = 18)
Hepatitis (N)	1	1
MRCP (N)	1(-)	1(-)
Preop ERCP	2(1+, 1-)	9(3+, 6-)
Intraop Cholangiogram	0	3 (-)
Resolved	1	4

Table 5.

Pathologic Findings

	Acute	Chronic
Mean wall thickness (mm)	5.7*	2.9
Quantity of stones†	2	2
Presence of Fibrosis†	2.8	1.0
Presence of Muscle†	2	0.7
Presence of inflammation cells†	3	1.2
Rokitansky-Aschoff†	1.7	1.7

*Student *t* test, $P \leq 0.0001$

†Graded on scale 0 to 4

function were worked up by intraoperative cholangiography (for liver function elevation, common bile duct dilation, and gallstone pancreatitis), and 12 patients had preoperative ERCP. Both MRCPs and 8 ERCPs were negative. Eight patients had sphincterotomies.

Other radiologic data included preoperative hepato-imino-diacetic acid (HIDA) scans and sonograms, which showed gallstones. In addition, comments were made during sonography regarding ductal dilatation (n = 5 chronic, ERCP [n = 2 (-), n = 1(+)], impacted cystic duct (n = 4 acute, n = 8 chronic), thickened wall (n = 4 acute, n = 10 chronic), and contracted gallbladder wall (n = 4 chronic). Of the acute cases, the 2 HIDA scans done were positive, 9 chronic cases were positive, and 8 were negative.

Pathology findings of inflammation, wall thickness, and quantity of stones were each predictive of operative time using single variable analysis (**Table 5**). Mean wall thickness of acute cases was greater than chronic ones, but did not remain a significant predictor of operative time using the adjusted multiple regression testing.

Conversion necessary in 1 acute case was due to the inability to grasp the gallbladder. Hydrops was aspirated in 4 acute and 3 chronic cases, bile spill was more likely in acute cases, and drains were used rarely (**Table 2**). Postoperative ERCP was done on 2 chronic cases. One case had a retained common bile duct stone with no preoperative liver function elevation; the patient was treated by sphincterotomy with resolution. The other had a cystic duct leak and was treated by placement of a 10 French stent.

DISCUSSION

Most reviews of laparoscopic cholecystectomy define cholecystitis by symptomatology rather than pathology. Regardless of the presence of calculi, right upper quadrant pain and tenderness, fever, and elevated white blood cell count are classically agreed upon clinical criteria for acute cholecystitis.⁶ Chronic cholecystitis is more a morphologic rather than a clinical entity, and it is unclear as to the exact time frame of its evolution.⁷ The presence of gallstones in the absence of acute inflammation is generally sufficient justification for the procedure diagnosis.

The distinction between pathologies can be difficult to make. The pathogenesis of both seems to be biochemical in nature, though sudden cystic duct obstruction is associated with acute cholecystitis. Both acute and chronic cholecystitis gallbladder walls are thickened, one with mural edema and hypervascularity, the other with fibrosis, coarse mucosal folds, muscular hyperplasia and Rokitansky-Aschoff sinuses (mucosal diverticula between

muscle fascicles). Hydrops or mucocele of the gallbladder is associated with prolonged obstruction of the cystic duct. Neither has infiltration of polymorphonucleocytes as a necessary significant finding, as their presence denotes at least 3 days into injury. Both acute and chronic cholecystitis may or may not have bacterial infection involved. The degree of inflammatory reaction is quite variable in chronic cases ranging from scattered lymphocytes, plasma cells, and macrophages to monocellular infiltrated fibrous tissue subepithelially and subserosally. Acute exacerbation of a previously chronically injured gallbladder may have evidence of all changes.^{8,9} Reviews of acute cases as done by Estes et al³ reveal that only one third of acute cases actually had pathologic changes diagnostic of acute cholecystitis, as their criteria required mural infarction, and polymorphonuclear cell infiltration. Pickelman and Gonzalez¹⁰ had a 39% discrepancy in clinical versus pathologic acute cases. This review also showed varied pathologic features among cholecystitis cases, showing a range of chronic inflammation and fibrosis even in acute cases. This most likely explains why acute cases were found at operation lagging even 5 weeks after diagnosis. Though clinically the patients were not exhibiting “acute” systemic signs of cholecystitis, their gallbladders pathologically had not recovered from their initial attack and continued to have the physical changes of “acute” cholecystitis. Our parameters of thick walls, numerous stones, and evidence of chronic inflammation each individually were associated with longer operative times; however, by multiple regression analysis these factors were less significant in determining operative time. All laparoscopic cholecystectomy cases had similar outcomes, regardless of thickened gallbladder walls, hypervascularity, chronic inflammation, and possible bacterial infection.

Laparoscopic cholecystectomy when introduced in 1989 was contraindicated in acute cases due to higher complication rates. However, over the years, numerous studies have challenged that assumption and the low threshold for conversion to open surgery, driven possibly by cost containment. Prior to laparoscopy, this was a leading argument in the debate of early versus delayed open cholecystectomy. Prospective data showed evidence that delayed cholecystectomy was associated with a 24% recurrence rate for acute cholecystitis during the interval from discharge to subsequent readmission. Early cholecystectomy was traditionally advised to avert the complications of gangrene, perforation, fistula formation, pan-

creatitis, choledocholithiasis, and particularly in medically treated patients who failed to resolve their symptoms within 72 hours. This review supports the view that even though symptoms resolve, the pathology may be acute even in the month following presentation and technically may pose a challenge to visualization.

Cholecystectomy for acute cases is associated with a higher complication rate in both open and laparoscopic cases. Conversion rates reported in the literature vary between 7% and 60% and are most commonly done for inability to define anatomy of the cystic duct because of inflammation and adhesion. Our 1 acute gangrenous cholecystitis patient underwent a laparotomy without laparoscopic dissection and was excluded from analysis because a laparoscopic cholecystectomy was not performed. Laparoscopic cholecystectomy for gangrenous cholecystitis in our practice is contraindicated.

The most common injury found in laparoscopic cholecystectomy is the cystic duct leak, which can be attributed to various causes.¹¹ Our cystic duct leak was most likely related to insufficient ligation of a short cystic duct stump.

Liver function test elevation and its prediction of longer operative time are related to numerous factors. These include extra time for intraoperative imaging, and technically handling the sequela of preoperative hepatitis, pancreatitis, and either spontaneously or iatrogenically resolved (by ERCP with sphincterotomy) choledocholithiasis. Obesity, diabetes, parity, sex, pretreatment with antibiotics, and prior abdominal surgery did not significantly affect the length of operative time.

Our study has some limitations. Although we adjusted for multiple variables that may have affected operative time, our retrospective review is small, with some missing data points, and unmeasured confounding variables may have been present.

CONCLUSIONS

Laparoscopic cholecystectomy can be done safely for both acute and chronic cases of cholecystitis. Operative time is similar. Abnormal liver enzymes are associated with longer operative times and should be considered preoperatively. Delay in operation had no effect on the length of operation.

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