Should Delayed Cholecystectomy Following Acute Calculous Cholecystitis Be Discouraged in a Resource-restricted Setting?

PA Leake¹, PO Roberts¹, K Pitzul², JM Plummer¹

ABSTRACT

Background: Early cholecystectomy for acute calculous cholecystitis (ACC) reduces hospital stay and complications during the waiting period. The purpose of this study is to establish the patterns of management of ACC at the University Hospital of the West Indies (UHWI) and to evaluate the advantages of early versus delayed cholecystectomy.

Methods: This was a retrospective chart review of patients admitted with a diagnosis of ACC. Data collection included demographics, management strategy, timing to cholecystectomy, significant events while awaiting cholecystectomy and duration of hospital stay. Mann-Whitney U and Chi-square tests were used for analysis. P-value of < 0.05 was considered significant.

Results: A total of 102 patient charts were extracted, 59 of which were managed conservatively and 43 managed with early cholecystectomy. The mean time to surgery after conservative management was 173 days. About 30% of persons managed conservatively had significant attacks while awaiting surgery, which included need for re-admission and earlier intervention. There was a trend toward longer mean total hospital stay in the conservative group ($x_{sx} = 5.03$, $x_{Cons} = 6.12$; p = 0.054).

Conclusion: Conservative management of ACC results in significant delays in definitive management and risks of complications during the waiting period. Early cholecystectomy should be encouraged even in a resource-restricted setting.

Keywords: Acute, anastomosis, calculous cholecystitis, cholecystectomy, colorectal, leakage

¿Debe Desalentarse la Colecistectomía Retardada después de una Colecistitis Calculosa Aguda en un Entorno de Recursos Limitados?

PA Leake¹, PO Roberts¹, K Pitzul², JM Plummer¹

RESUMEN

Antecedentes: La colecistectomía temprana en el caso de la colecistitis calculosa aguda (CCA) reduce la estancia hospitalaria y las complicaciones durante el período de espera. El propósito de este estudio es establecer las normas para el manejo de la CCA en el Hospital Universitario de West Indies (HUWI), así como evaluar las ventajas de la colecistectomía temprana frente a la colecistectomía retardada. Métodos: Se trató de un estudio retrospectivo de las historias clínicas de pacientes ingresados con diagnóstico de CCA. Los datos recopilados incluyeron información demográfica, estrategia de manejo, tiempo para la colecistectomía, eventos significativos en la espera de la colecistectomía, y duración de la estancia hospitalaria. Se utilizaron Pruebas U de Mann-Whitney y Chi-cuadrado para el análisis. El valor P de < 0.05 se consideró significativo.

Resultados: Se extrajeron un total de 102 historias clínicas de pacientes, 59 de los cuales fueron tratados de manera conservadora y 43 tratados con colecistectomía temprana. El tiempo promedio para la cirugía tras el manejo conservador fue de 173 días. Aproximadamente el 30% de las personas tratadas de manera conservadora tuvieron ataques significativos mientras se esperaba la cirugía, que incluía la necesidad de reingreso y de intervención más temprana. Hubo una tendencia a un promedio total más largo de estancias hospitalarias en el grupo conservador ($x_{sx} = 5.03$, $x_{Cons} = 6.12$; p = 0.054).

From: ¹Department of Surgery, Radiology, Anaesthesia and Intensive Care, Faculty of Medical Sciences, The University of the West Indies, Kingston 7, Jamaica and ²Institute of Health Policy Management and Evaluation, University of Toronto, Toronto, Ontario, Canada M5T 3M6.

Correspondence: Dr PA Leake, Department of Surgery Radiology, Anaesthesia and Intensive Care, Faculty of Medical Sciences, The University of the West Indies, Kingston 7, Jamaica, West Indies. E-mail: paeleake@yahoo.com

Leake et al 389

Conclusión: El manejo conservador de la CCA trae como resultado retrasos significativos en el manejo definitivo y riesgos de complicaciones durante el período de espera. Se recomienda la colecistectomía temprana incluso en un entorno de recursos limitados.

Palabras claves: Aguda, anastomosis, colecistitis calculosa, colecistectomía, colorrectal, fuga

West Indian Med J 2015; 64 (4): 389

INTRODUCTION

Acute calculous cholecystitis (ACC) is one of the most common emergencies in general surgery. Its course may range from mild inflammation (grade I/mild) to fulminant infection (empyema, gangrene, perforation – grade II/moderate) and systemic organ dysfunction [grade III/severe] (1). Current best practice for moderate and severe ACC is urgent intervention (either cholecystectomy or drainage). However, the best practice for treatment of mild ACC varies. Patients may either be managed with a period of conservative treatment (nil by mouth status, analgesia +/- antibiotics) followed by delayed cholecystectomy at least six weeks later or they are managed by early cholecystectomy [usually in the index admission] (2).

Randomized controlled trials and meta-analyses of early laparoscopic cholecystectomy *versus* conservative treatment with delayed cholecystectomy for ACC have demonstrated that although both options are safe, early cholecystectomy results in overall shorter hospital stay and reduced risk of significant attacks during the waiting period for elective surgery while not

increasing surgical morbidity and mortality (3–12). The Tokyo Guidelines recommend early laparoscopic cholecystectomy for mild and moderate ACC (13).

Conservative management with delayed cholecystectomy is a viable and safe option for the treatment of ACC, and early cholecystectomy can place an additional resource burden on an already limited system. Therefore, choosing between these two treatment options can be difficult in a resource-restricted setting. The purpose of this study is to describe the practice patterns and outcomes of management of mild ACC at an institution in a resource-restricted setting.

SUBJECTS AND METHODS

This is a retrospective chart review of all patients admitted to the surgical service of the University Hospital of the West Indies (UHWI) with a diagnosis of mild ACC between January 2008 and December 2010. The Tokyo Guidelines (1) were used to identify patients with mild ACC (Table 1). Patients aged < 12 years, diagnosed with moderate or severe acute

Table 1: Criteria for acute cholecystitis based on the Tokyo Guidelines (1)

Mild (grade I) acute cholecystitis

"Mild (grade I)" acute cholecystitis does not meet the criteria of "severe (grade III)" or "moderate (grade II)" acute cholecystitis. Grade I can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and only mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure.

Moderate (grade II) acute cholecystitis

"Moderate" acute cholecystitis is accompanied by any one of the following conditions:

- 1. Elevated white blood cell count (> 18000/mm³)
- 2. Palpable tender mass in the right upper abdominal quadrant
- 3. Duration of complaints > 72 hours
- Marked local inflammation (biliary peritonitis, pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, emphysematous cholecystitis)

Severe (grade III) acute cholecystitis

"Severe" acute cholecystitis is accompanied by dysfunctions in any of the following organs/systems:

- Cardiovascular dysfunction (hypotension requiring treatment with dopamine ≥ 5 ug/kg per min, or any dose of dobutamine)
- Neurological dysfunction (decreased level of consciousness)
- 3. Respiratory dysfunction (PaO₂/FiO₂ ratio < 300)
- Renal dysfunction (oliguria, creatinine > 2.0 mg/dL)
- 5. Hepatic dysfunction (PT-INR > 1.5)
- Haematological dysfunction (platelet count < 10000/mm³)

cholecystitis, who underwent emergency cholecystectomy, or who were diagnosed with acalculous cholecystitis were excluded.

Data collection included patient demographics, management strategy, timing to cholecystectomy, surgical approach (open or laparoscopic), operative time, conversion rate (for laparoscopic cases), complications, total hospital stay (inclusive of cancelled operations) and the nature of significant attacks while awaiting surgery. Patients were separated into two groups – conservative management with delayed cholecystectomy and early cholecystectomy (surgery during the index admission).

Statistical analysis performed aimed to determine the differences between groups with respect to surgical approach, operative time, conversion rate, complications and total hospital stay. The frequency and nature of attacks while awaiting surgery and the default rate were also determined. Mann-Whitney U and Chi-squared tests were used for non-parametric scale and categorical variables, respectively. *P*-value of < 0.05 was considered significant.

RESULTS

During the two-year study period, 116 admissions were identified. Fourteen cases were excluded due to legitimate reasons for conservative management, including evidence of choledocholithiasis and uncontrolled co-morbidities with high anaesthetic risk. Therefore, 102 cases were included in the analysis.

Fifty-nine patients were managed conservatively (Table 2).

Of this group, 25 went on to have delayed cholecystectomy (Table 2). Twenty-three patients had not had surgery or had defaulted from follow-up (Table 3).

There were no differences between groups with respect to age, gender distribution, operating time, complications or conversions (Table 2). Twenty of 25 patients undergoing delayed cholecystectomy had a laparoscopic approach as compared to 12 of 43 patients in the early cholecystectomy group (Table 2; p < 0.001). There was a trend toward longer total hospital stay (including cancelled operations) in the conservative group (6.12 days) as compared to the early cholecystectomy group (5.03 days; p = 0.054).

The mean time to delayed cholecystectomy following conservative management was 173 days. During this waiting period, 18 of 59 (30.5%) patients had a significant episode related to cholelithiasis, warranting either a visit to the emergency room and/or hospital admission. These significant attacks included 14 episodes of biliary colic, 11 episodes of acute cholecystitis, two episodes of acute pancreatitis and one episode of choledocholithiasis. There was no associated mortality related to these attacks.

DISCUSSION

The present study demonstrates that the majority of patients with mild ACC are being managed conservatively at our institution, with a view to undergoing delayed cholecystectomy. A

Table 2: Patient distribution and outcome measures according to management of acute calculous cholecystitis

	Conservative management with delayed cholecystectomy	Early cholecystectomy	P-value
Γotal number of cases	59	43	-
Mean (± SD) age (years)	39.39 (12.86)	40.47 (13.9)	0.688
Male [n/total n]	5/59	6/43	0.776
Laparoscopic [n/total n]	20/25	12/43	< 0.001
Mean (± SD) duration of operation (minutes)	120.00 (10.61)	156.83 (59.85)	0.395
Mean (± SD) length of stay (days)	6.12 (2.74)	5.03 (1.95)	0.054
Complication [n/total n]	2/25	2/43	-
Converted [n/total n]	2/20	2/12	

Table 3: Disposition of patients managed conservatively who had not undergone delayed cholecystectomy

Disposition	Number of patients
Re-admission for repeat attack with early or emergency cholecystectomy	7
Failed conservative management – required early cholecystectomy	2
Not yet had surgery at completion of study	17
Defaulted from follow-up	6
Missing information	2

Leake et al 391

significant proportion of these patients still had not undergone their cholecystectomy or had defaulted from follow-up by the end of the study time-frame. During the waiting period for surgery, a large proportion of this group required re-admission or a visit to hospital. Laparoscopic cholecystectomy is the predominant approach for delayed cholecystectomy but is an uncommon approach in the acute setting.

Current evidence is conflicting regarding whether or not conservative management with delayed cholecystectomy remains an appropriate option for the management of mild ACC (14–16). In the era of open cholecystectomy, randomized trials demonstrated that early cholecystectomy was safe and provided the advantages over delayed cholecystectomy of costeffectiveness, reduced operative time, complication rate, hospital stay and return to normal activity (17-20). Since the establishment of laparoscopic cholecystectomy as the standard of care for elective gall bladder surgery (21), attention has turned to its use in the acute setting. The advantage of shorter hospital stay has been established while concerns regarding increased complication rates and conversion rates have been dispelled by randomized controlled trials and meta-analyses (3–12). In addition, up to 20% of patients will fail conservative management and up to 25% of patients will relapse while awaiting definitive surgery (22), contributing to morbidity and increased costs and further favouring early cholecystectomy. The overwhelming evidence has resulted in guidelines recommending early cholecystectomy as preferable in the management of mild ACC (13).

Despite the evidence, the global uptake of early chole-cystectomy is low. In the United Kingdom, only 11% of surgeons routinely treated patients with early cholecystectomy (23). In Japan, even following the institution of the Tokyo Guidelines, only 41.7% to 62.3% of surgeons opted for early cholecystectomy (24). These results are consistent with our study findings, which demonstrate that conservative management followed by delayed cholecystectomy is the most common management approach for patients with mild ACC at our institution.

There are clearly barriers to early cholecystectomy in resource-restricted settings. Internationally, surgeon surveys have cited unavailability of staff, lack of theatre space and time, concerns about missing the window period (with increased complications) and staff reluctance due to variability in surgeon practice (23, 25) as common barriers. We believe that concerns regarding the appropriate use of resources, limited operating time and the attitudes of staff play the most important roles in our setting.

With current evidence supporting laparoscopy as the standard of care of gall bladder surgery (21) and laparoscopic cholecystectomy as the ideal approach to early cholecystectomy (13), there are increased expectations from patients for the use of laparoscopy, even in resource-restricted settings. However, there is limited laparoscopic equipment at our institution. As such, there are genuine concerns about the increased

use of such equipment, with risk of 'wear and tear', in the acute setting. Surgeons may opt for a delayed approach to laparoscopic cholecystectomy as a compromise to this issue. Limited operating time does not allow for patients undergoing early cholecystectomy to be placed on an elective list. These patients are likely to be placed on an emergency list. It may be argued that these patients are not true emergencies, can be managed non-operatively and that emergency operating time is being used injudiciously. In any institution where laparoscopy is new and open surgery is the current standard of care, there will be potential resistance to change from staff members. Laparoscopy is used rarely in our institution for emergency procedures. Such an approach is associated with longer operating times and can be criticized as inappropriate in a resource-restricted setting.

Understanding the barriers to early cholecystectomy is critical and requires further study. It is possible that the desire to offer patients a laparoscopic approach takes precedence over offering early cholecystectomy. Naraynsingh *et al* suggested an alternative that may be applicable in such a situation: a mini-laparotomy cholecystectomy, where an open incision of median length 4.8 cm, appeared to offer similar benefits to laparoscopic cholecystectomy (26). Additional research is required to further describe the use of mini-laparotomy in this setting.

Our study demonstrated that despite conservative management being an effective option for the management of mild ACC (only two patients failed conservative management), this approach is not innocuous. Compared to current evidence, the surgical wait time was at the higher end of the currently reported range, resulting in a large proportion of patients experiencing relapse while awaiting surgery (14, 15, 27). Furthermore, the risk of significant interval attacks requiring readmission or intervention fell within the reported ranges of 14.0% to 35% previously published (14, 16, 27–30). This results not only in morbidity, but increased overall costs (28) which is a significant issue in an already resource-restricted setting.

A significant proportion of patients managed conservatively either had not had surgery or had defaulted from follow-up. Cultural views regarding fears of surgery (31) are likely to play a significant role. In addition, lack of operating time and cancellations are common-place in resource-restricted settings (32). These factors must be considered as part of surgeons' decision-making at the time of initial management.

This study is not without limitations. This is a retrospective study and is therefore not immune to errors from data abstraction. A second abstractor reviewed patients' charts to ensure consistency of the information collected. In addition, no data were collected on the rationale for management approach, including patient preference (*eg* cultural views) and limiting circumstances in the hospital setting (*eg* laparoscopic equipment availability, operating theatre availability). This information would have allowed for further interpretation of the results.

The evidence discouraging conservative management of mild ACC and delayed cholecystectomy is strong. Our study supports the detrimental effects of such an approach. As such, early cholecystectomy should be encouraged even in a resource-restricted setting. We recognize that a laparoscopic approach to early cholecystectomy is recommended. Future work should focus on the identification of the barriers limiting the use of early laparoscopic cholecystectomy and provide context-specific solutions.

REFERENCES

- Hirota M, Takada T, Kawarada Y, Nimura Y, Miura F, Hirata K et al. Diagnostic criteria and severity assessment of acute cholecystitis: Tokyo Guidelines. J Hepatobiliary Pancreat Surg 2007; 14: 78–82.
- Brunicardi FC. Schwartz's Principles of Surgery. In: Brunicardi FC, editor. Schwartz's Principles of Surgery. 9th ed. Unites States of America: The McGraw-Hill Companies, Inc; 2010: 2160–239.
- Lai PB, Kwong KH, Leung KL, Kwok SP, Chan AC, Chung SC et al. Randomized trial of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Br J Surg 1998; 85: 764–7.
- Lo CM, Liu CL, Fan ST, Lai EC, Wong J. Prospective randomized study of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Ann Surg 1998; 227: 461–7.
- Serralta AS, Bueno JL, Planells MR, Rodero DR. Prospective evaluation of emergency versus delayed laparoscopic cholecystectomy for early cholecystitis. Surg Laparosc Endosc Percutan Tech 2003; 13: 71–5.
- Johansson M, Thune A, Blomqvist A, Nelvin L, Lundell L. Impact of choice of therapeutic strategy for acute cholecystitis on patient's healthrelated quality of life. Results of a randomized, controlled clinical trial. Dig Surg 2004; 21: 359–62.
- Kolla SB, Aggarwal S, Kumar A, Kumar R, Chumber S, Parshad R et al. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a prospective randomized trial. Surg Endosc 2004; 18: 1323-7
- Shikata S, Noguchi Y, Fukui T. Early versus delayed cholecystectomy for acute cholecystitis: a meta-analysis of randomized controlled trials. Surg Today 2005; 35: 553–60.
- Lau H, Lo CY, Patil NG, Yuen WK. Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis. Surgical Endosc 2006: 20: 82–7.
- Gurusamy KS, Samraj K. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Cochrane Database Syst Rev 2006; 4: CD005440.
- Siddiqui T, MacDonald A, Chong PS, Jenkins JT. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis of randomized clinical trials. Am J Surg 2008; 195: 40–7.
- Chandler CF, Lane JS, Ferguson P, Thompson JE, Ashley SW. Prospective evaluation of early versus delayed laparoscopic cholecystectomy for treatment of acute cholecystitis. Am Surg 2000; 66: 896–900.
- 13. Yamashita Y, Takada T, Kawarada Y, Nimura Y, Hirota M, Miura F et al.

- Surgical treatment of patients with acute cholecystitis: Tokyo Guidelines. J Hepatobiliary Pancreat Surg 2007; **14:** 91–7.
- Cheruvu CV, Eyre-Brook IA. Consequences of prolonged wait before gallbladder Surgery. Ann R Coll Surg Engl 2002; 84: 20–2.
- Glasgow RE, Cho M, Hutter MM, Mulvihill SJ. The spectrum and cost of complicated gallstone disease in California. Arch Surg 2000; 135: 1021–5; discussion 5–7.
- Rutledge D, Jones D, Rege R. Consequences of delay in surgical treatment of biliary disease. Am J Surg 2000; 180: 466–9.
- Lahtinen J, Alhava EM, Aukee S. Acute cholecystitis treated by early and delayed surgery. A controlled clinical trial. Scand J Gastroenterol 1978; 13: 6738.
- van der Linden W, Sunzel H. Early versus delayed operation for acute cholecystitis. A controlled clinical trial. Am J Surg 1970; 120: 7–13.
- 19. Jarvinen HJ, Hastbacka J. Early cholecystectomy for acute cholecystitis: a prospective randomized study. Ann Surg 1980; 191: 501–5.
- Norrby S, Herlin P, Holmin T, Sjodahl R, Tagesson C. Early or delayed cholecystectomy in acute cholecystitis? A clinical trial. Br J Surg 1983; 70: 163–5.
- Keus F, de Jong JA, Gooszen HG, van Laarhoven CJ. Laparoscopic versus open cholecystectomy for patients with symptomatic cholecystolithiasis. Cochrane Database Syst Rev 2006; 4: CD006231.
- Gananadha S, Fergusson J. Moderate acute cholecystitis: to cut now or to cut later. J Gastroenterol Hepatol 2009; 24: 1806–7.
- Cameron IC, Chadwick C, Phillips J, Johnson AG. Management of acute cholecystitis in UK hospitals: time for a change. Postgrad Med J 2004; 80: 292–4.
- Shinya S, Yamashita Y, Takada T. The impact of the Japanese clinical guidelines on the clinical management of patients with acute cholecystitis. J Hepatobiliary Pancreat Sci 2013; 20: 611–9.
- Senapati PS, Bhattarcharya D, Harinath G, Ammori BJ. A survey of the timing and approach to the surgical management of cholelithiasis in patients with acute biliary pancreatitis and acute cholecystitis in the UK. Ann R Coll Surg Engl 2003; 85: 306–12.
- Naraynsingh V, Singh Y, Remy T, Hariharan S, Dan D. Minilaparotomy cholecystectomy – an appropriate alternative to laparoscopic cholecystectomy in developing nations. Trop Gastroenterol 2010; 31: 312–6.
- Lawrentschuk N, Hewitt PM, Pritchard MG. Elective laparoscopic cholecystectomy: implications of prolonged waiting times for surgery. A N Z J Surg 2003; 73: 890–3.
- Somasekar K, Shankar PJ, Foster ME, Lewis MH. Costs of waiting for gall bladder surgery. Postgrad Med J 2002; 78: 668–9.
- 29. de Mestral C, Rotstein OD, Laupacis A, Hoch JS, Zagorski B, Nathens AB. A population-based analysis of the clinical course of 10,304 patients with acute cholecystitis, discharged without cholecystectomy. J Trauma Acute Care Surg 2013; 74: 26–30; discussion 30–1.
- Gurusamy K, Samraj K, Gluud C, Wilson E, Davidson BR. Meta-analysis
 of randomized controlled trials on the safety and effectiveness of early
 versus delayed laparoscopic cholecystectomy for acute cholecystitis. Br
 J Surg 2010; 97: 141–50.
- McGaw CD, Hanna WJ. Knowledge and fears of anaesthesia and surgery. The Jamaican perspective. West Indian Med J 1998; 47: 64–7.
- Jonnalagadda R, Walrond ER, Hariharan S, Walrond M, Prasad C. Evaluation of the reasons for cancellations and delays of surgical procedures in a developing country. Int J Clin Pract 2005; 59: 716–20.