Chronic Acalculous Gallbladder Disease: Outcomes of Treatment by Laparoscopic Cholecystectomy

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Abstract

Background and aims. The diagnosis and treatment of chronic acalculous gallbladder disease (CAGD) remains controversial. Laparoscopic cholecystectomy (LC) is increasingly accepted as the treatment of choice for this condition. The purpose of this study was to analyse the outcomes from LC for CAGD and to identify potential prognostic factors.

Methods. We retrospectively analysed 54 patients with a clinical diagnosis of CAGD. All patients underwent LC. The outcomes were evaluated at 12 months. Outcomes from surgery were graded on a predetermined scoring system (score 1-6) reflecting the effect of surgery on symptomatology. Histopathological analysis was systematically performed on the resection specimens.

Results. Post-operatively, 90.8% of patients (49/54) were satisfied with the operation (outcome score 1-2). A pathological abnormality was detected in 40 patients (74.1%). Of those in whom no abnormality detected on histopathological examination, LC achieved a successful outcome (score 1-2) in 85.7% of patients (12/14). The worst outcomes (score 5-6) were observed in 2 patients with a pathological abnormality of the gallbladder. For the 5 patients with outcome scores of 3 to 6 (poor outcome), the mean duration of symptoms was 7.1 months compared to 18.2 months for patients with score of 1 and 2 (good outcome).

Conclusions. There is no significant correlation between outcomes from LC for CAGD and the existence of a definable underlying pathology ($p>0.05$). Patients with long-standing symptoms were more likely to benefit from LC ($p=0.039$). LC is an appropriate treatment option for CAGD.

Key words

Chronic acalculous gallbladder disease - laparoscopic cholecystectomy - prognostic factors - outcomes

Rezumat

Introducere. Diagnosticul şi tratamentul bolii veziculare cronice acalculoase (BVCA) rămâne controversat. Colecistectomia laparoscopică (CL) este din ce în ce mai frecvent propusă pentru tratamentul acestei afecţiuni. Scopul acestui studiu a fost de a analiza rezultatele CL pentru BVCA şi de a identifica potenţiali factori prognostici ai rezultatelor.

Material şi metodă. Cincizeci şi patru de pacienţi cu diagnostic clinic de BVCA au fost analizaţi retropectiv. Toţi pacienţii au beneficiat de CL. Evaluarea rezultatelor a fost făcută la 12 luni. Rezultatele postoperatorii asupra simptomatologiei au fost evaluate pe o scala predeterminată de la 1 la 6, 1 reprezentând dispariţia completă a simptomelor, iar 6 agravarea simptomelor cu apariţia de simptome noi.

Rezultate. Postoperator, 49 de pacienţi (90,8%) s-au declarat satisfăcuţi de rezultate (scor 1 şi 2). Examenul histopatologic a identificat în 40 de cazuri (74,1%) anomalii ale veziculei biliare. Pentru 85,7% din pacienţii cu examen histologic normal CL a condus la rezultate bune. Rezultatele cele mai slabe (scor 5 şi 6) au fost obţinute pentru 2 pacienţi ce prezentau leziuni ale veziculei biliare. Pentru cei 5 pacienţi cu scor mai mare de 3, durata medie a simptomelor anterior chirurgiei a fost de 7,1 luni comparată cu 18,2 luni pentru pacienţii cu scor 1 şi 2.

Concluzii. Nu se poate spune că există o corelaţie între rezultatele CL pentru BVCA şi datele histopatologice ($p>0,05$). Pacienţii cu simptome de durată mai lungă sunt mai înclinaţi de a răspunde favorabil la CL ($p=0,039$). Colecistectomia laparoscopică reprezintă o opţiune viabilă de tratament pentru aceşti pacienţi.

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Introduction

Chronic acalculous gallbladder disease (CAGD) is a controversial clinical entity, the aetiology of which is not fully understood. Chronic acalculous cholecystitis, biliary dyskinesia, acalculous biliary colic are terms which define an entity characterized by post-prandial recurrent biliary pain (right upper quadrant), nausea and intolerance to fatty food in the absence of cholelithiasis and other pathologies which may explain the symptoms. Currently, there are no strict diagnostic criteria for CAGD, which is diagnosed by exclusion of other pathologies, in particular, upper gastrointestinal disorders. The definitive diagnosis can only be made retrospectively by the pathologist. The incidence of CAGD has been reported to be 5% of all patients undergoing cholecystectomy (1,2). Recently, with the growing popularity of laparoscopic cholecystectomy (LC), the pathological data reveal that this entity is more frequently encountered than previously thought (2-4). LC has been shown to achieve good results in patients with chronic biliary symptoms (3-8). The purpose of this paper was to evaluate the clinical outcome following LC in patients with a clinical diagnosis of CAGD in order to identify factors which may influence prognosis.

Patients and methods

A total of 54 patients admitted and operated in the Emergency Surgical Clinic, Iaşi between January 2002 and December 2003 were analysed. Patients with signs and symptoms of CAGD, a normal ultrasound examination and no other identifiable cause of the symptoms were included in the study. Special investigations such as cholecystokinin-stimulated scintigraphy (CCK-HIDA) or symptom-reproducing tests with cholecystokinin were not performed. All patients with gallstones detected on ultrasound, morphological anomalies of the biliary anatomy or acute symptoms were excluded from the study. In addition, patients with lower gastrointestinal symptoms suggestive of irritable bowel syndrome (IBS) were excluded from the study and managed by an alternative method.

All 54 patients included in the study underwent LC electively. All gallbladder specimens were available for histopathological review. Hospital charts were retrospectively reviewed to obtain preoperative data including demographic data, duration of symptoms, results of investigations and previous treatments. Intraoperative data collected included macroscopic evaluation and operative procedure. Post-operative data included post-operative course, hospital stay, complications and results from histopathological examination. The patients were followed-up periodically, the outcome being evaluated at 12 months. A scoring system was used to categorize the outcome from surgery using a predetermined scale ranging from 1 to 6 (1 – complete remission of symptoms following procedure, 6 – worsening of symptoms and emergence of new symptoms), which reflected the effect of surgery on symptomatology. A score of 1 or 2 was considered as a good outcome and 3 to 6 as a poor outcome. Statistical analysis was performed using the standard Student *t*-Test and Chi-squared test for categorical data. A value of $p<0.05$ was considered as statistically significant.

Results

Fifty-four patients underwent LC for CAGD. There were 45 women (83.3%) and 9 men (16.6%), the average age being 44.6 years (range 23-69 years). The median duration of symptoms before surgery was 1 year and 3.3 months (range 3 months – 4 years and 1 month). All patients had at least one admission to hospital for diagnostic investigations prior to surgery. The final diagnosis was established based on clinical symptoms, a negative ultrasound scan and exclusion of other pathologies. Seven patients had a CCK-HIDA test although this was not included in the preoperative criteria for diagnosis. Commonly encountered symptoms in our series included recurrent post-prandial right upper quadrant pain associated with nausea (100%), fat intolerance (61.8%) and bloating (35.2%). The preoperative investigations performed are shown in Table I.

Table I Preoperative investigations

Preoperative investigation	No. patients (%)	No. investigations-No. patients (%)
Ultrasound	54(100)	2-54(100) 3-22(40.7) 4-10(18.5) 5-8(14.8) 6-1(1.8)
Upper gastrointestinal endoscopy	54(100)	2-3(5.5) 3-1(1.8)
Upper gastrointestinal contrast study	38(70.4)	2-2(3.7) 3-1(1.8)
Colonoscopy	21(38.9)	2-2(3.7) 3-1(1.8)
Barium enema	19(35.2)	2-1(1.8)
Abdominal computed tomography	23(42.6)	2-1(1.8) 3-1(1.8)
Endoscopic retrograde cholangiopancreatography	8(14.8)	-
Intravenous urography	11(20.8)	-
CCK-HIDA test	7(13)	-

All patients had at least two ultrasound examinations on separate occasions performed by different senior echographists. As evident in Table I, all patients had upper gastrointestinal endoscopy to exclude other causative pathologies. The most frequent preoperative diagnoses encountered comprised biliary dyskinesia (20 patients), chronic acalculous cholecystitis (28 patients), chronic gastritis (3 patients), chronic gastroduodenitits (3 patients) and gastro-oesophageal reflux disease (17 patients). More than one diagnosis was reached preoperatively in a number of patients. All patients received a variety of medical treatments prior to surgery - 17 of them received a proton pump inhibitor and 4 had *Helicobacter pylori* eradication. Despite this, the symptoms persisted in all patients.

All patients underwent LC as an elective procedure. There were no conversions to open surgery and no intraoperative complications. Adhesiolysis was performed in two patients. The mean hospital stay was 3.3 days. No patients were discharged on the day of the operation. No patients were readmitted to hospital for postoperative problems. Two patients developed postoperative complications which were directly related to surgery – one patient developed a parietal haematoma (umbilical site) and one patient developed acute urinary retention. The outcomes were evaluated at 12 months. The postoperative outcome scores are shown in Table II.

Table II Outcomes of laparoscopic cholecystectomy for CABD

Symptoms	Score	No. patients (%)
Complete absence	1	38 (70.4)
Significant improvement	2	11 (20.4)
Persistence	3	2 (3.7)
New	4	1 (1.8)
Worsening	5	1 (1.8)
New and worsening	6	1 (1.8)

As evident in Table II, 49 patients (90.8%) had good outcome from the operation (score 1 and 2). Two patients (3.7%) had persistence of symptoms (score 3) and 3 patients (5.6%) were worse after surgery (score 4-6).

Histopathological diagnosis was reached in all patients: 33 chronic inflammation of the gallbladder, 14 normal gallbladder and 7 cholesterolosis. Table III shows the relationship between outcomes and the results of histopathological examination.

Table III Relationship between outcome and histopathological examination

Histopathological result (no. patients)	Score	No. patients
Chronic inflammation (33)	1	24
	2	7
	3	1
	4	-
	5	-
	6	1
Normal gallbladder (14)	1	9
	2	3
	3	1
	4	1
	5	-
	6	-
Cholesterolosis (7)	1	5
	2	1
	3	-
	4	-
	5	1
	6	-

There was no significant difference between outcome from surgery and histopathological diagnosis ($p>0.05$). The average length of preoperative symptoms for patients with a poor outcome (scores 3-6) was 7.1 months compared to 18.2 months for patients with a good outcome (score 1-2), the difference reaching statistical significance ($p=0.039$).

Discussion

LC has now been accepted as the gold standard for the treatment of symptomatic gallstones. Since its introduction, this minimally invasive approach has become increasingly utilized for both calculous and acalculous gallbladder disease. CAGD represents a clinical entity which is not clearly defined and incorporates chronic inflammation, biliary dyskinesia, intrinsic motility disorders and functional disorders of biliary flow. Considering the diverse range of symptomatology and the variety of underlying pathologies, there are controversies regarding the diagnosis and treatment of CAGD. Part of the diagnostic work-up includes CCK-HIDA scan and CCK challenge test although the diagnostic values of these tests are uncertain. A fraction of ejection of less than 35%, which was considered as diagnostic for gallbladder disease, seems to have the same occurrence in asymptomatic people (9). Furthermore, a number of studies have shown that the results of CCK-HIDA test do not predict clinical outcomes after cholecystectomy (3,4,10). Clinical assessment therefore remains fundamental in the diagnosis of CAGD, some authors renouncing to do ancillary tests (6). Excluding other causes, in particular gastro-oesophageal reflux disease, remains an essential part of diagnostic work-up. In our study, the diagnosis was established for all 54 patients on clinical grounds. Great attention was paid to exclude gastro-oesophageal reflux disease - all patients received at least one upper gastrointestinal endoscopic examination, 38 patients (70.8%) also received a contrast meal and 17 patients were treated with proton pump inhibitors empirically prior to surgery.

Irritable bowel syndrome is one of the most common functional gastrointestinal disorders, the prevalence rate being 10-20% and women having a higher prevalence (11). Currently, it is difficult to differentiate non-specific upper gastrointestinal symptomatology from symptoms arising from IBS. IBS comprises a group of functional bowel disorders in which abdominal discomfort or pain is associated with a change in bowel habit, and with features of disordered defecation. Unlike CAGD, the clinical features of IBS are predominantly related to defecation. The diagnosis of IBS was considered in all patients recruited for the study according to the Rome Criteria (11,12). As this is also a diagnosis of exclusion, all patients with lower gastrointestinal symptoms suggestive of IBS were thoroughly investigated to exclude major identifiable diagnoses, and treated accordingly following exclusion from the study.

The success rate after LC for symptomatic gallstones is between 80-90% (13). Studies which have evaluated the benefits of LC for CAGD, have shown variable results, the success rate ranging between 70% (14) and 96% (6) for patients in whom the diagnosis was established clinically.

Histopathological analysis for CAGD reveals similar findings to calculous disease except for the presence of erosions and ulcerations secondary to gallstones. The diagnostic criteria for chronic cholecystitis are the presence of monocyte infiltration, fibrosis and metaplasia. Studies have shown that these inflammatory lesions are present in the gallbladder wall in 48-92% of cases of cholecystectomies performed for acalculous cholecystitis. There are also variations between the correlation of clinical symptoms with the underlying pathology (3-5,7). Studies have shown that LC improved symptoms not only in patients in whom inflammatory lesions were detected on histopathology. Patients with a normal histopathological examination have been associated with the complete cessation of symptoms following LC (3,4,6,8). In our study, 90.8% (49/54) of patients showed either absence or significant improvement of symptoms following LC (outcome score 1-2), which is comparable to previous data in the literature. Forty patients had abnormal histopathological examination. Of this, 37 (92.5%) had outcome score 1 and 2 after LC. Out of the 14 patients with a normal histopathological examination, 12 (85.7%) had a good outcome from the operation (score 1 and 2). Our series indicates that there is a lack of correspondence between improvement of symptomatology by LC and underlying pathology in CABD. The worse results (score 5-6) were seen in 2 patients, both of whom had an abnormality detected on histopathological examination (one patient with chronic cholecystitis, one patient with cholesterolosis). This again is in concordance with our conclusion that the presence of histopathological lesions does not correlate with successful outcomes following LC ($p>0.05$).

The best outcomes were observed in the patients with longer preoperative symptomatology. Frassinelli et al (4), in a series of 243 patients with acalculous cholecystitis established a direct relation between the length of symptoms and the outcomes after LC, patients with long-standing symptoms being more likely to respond favourably to operative treatment. In our series, for the five patients with poor outcome (score 3-6), the duration of symptoms was significantly shorter compared to those with good outcome (score 1-2), 7.1 months and 18.2 months respectively ($p=0.039$). This raises the question whether surgery should be considered in these patients immediately or following a long period of observation.

LC for patients with CAGD is performed in elective conditions with minimal operative risk. Only 2 patients (3.7%) had minor postoperative complications, which confirms that LC is a safe procedure in these patients.

In conclusion, LC offers a chance of cure for patients with CAGD, the outcomes being comparable with those obtained for calculous disease. Laparoscopic cholecystectomy can end a long history of diagnostic investigations and patient suffering and reduce the costs of managing such patients. Essential requirements for establishing the correct diagnosis are a thorough clinical assessment and the exclusion of other pathologies. We consider that a diagnosis of CAGD can be established based on a triad of biliary colic, normal ultrasound examination and exclusion of other diseases responsible for the symptoms. A precise clinical diagnosis seems to be adequate to predict outcome from operative treatment. There seems to be no correlation between outcomes and the presence of histopathological abnormalities. Patients with long-standing preoperative symptoms are more likely to improve with LC. The lower rate of complications after LC and good outcomes for patients with CAGD suggest that this approach is safe and effective in such patients.

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