Laparoscopic cholecystectomy for acalculous gallbladder disease

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Use of laparoscopic cholecystectomy (LC) to treat patients with symptoms due to gallstone disease is well established. However, use of LC for patients with acalculous gallbladder disease remains controversial. In this study, we examined the use of hepatobiliary iminodiacetic acid (HIDA) scans with cholecystokinin (CCK) infusion to identify patients with acalculous gallbladder disease who would benefit from LC. From December 1991 to February 1997, 4480 patients underwent cholecystectomy at Baylor University Medical Center, including 72 patients who underwent LC for acalculous disease following preoperative HIDA scan. We retrospectively analyzed their preoperative symptoms and workup. Follow-up was obtained by telephone questionnaire in 59 of 72 patients

(82%). Overall, 48 of 59 patients (82%) reported an excellent outcome following LC. We found no significant difference in outcome in patients who underwent HIDA scan with CCK infusion, regardless of gallbladder ejection fraction or exacerbation of symptoms caused by the infusion. Preoperative symptom complex was also not predictive of postoperative outcome. LC is an effective treatment for patients with acalculous gallbladder disease. A preoperative HIDA scan with CCK infusion does not accurately predict treatment success or failure. Patients with a normal ejection fraction and absence of symptoms from a HIDA scan can still have excellent relief of symptoms after LC.

Since its introduction in 1989, laparoscopic cholecystectomy (LC) has emerged as the treatment of choice for patients with symptomatic cholelithiasis, acute cholecystitis, and biliary pancreatitis (1). Preoperative workup of these patients is well established, and long-term relief of symptoms has been reported to approach 95% (2). However, preoperative workup and treatment for patients who present with symptoms of gallbladder disease but do not have gallstones remain unclear. Symptoms are usually consistent with biliary colic, such as right upper quadrant pain, epigastric pain, or postprandial nausea and vomiting. An exhaustive diagnostic workup with sonography, computed tomography scan, esophagogastroduodenoscopy, colonoscopy, endoscopic retrograde cholangiopancreatography, and upper gastrointestinal series may not provide an acceptable explanation for the patient's symptoms. Often there are long delays between initial presentation and final treatment.

The technetium 99 (⁹⁹Tc) hepatobiliary iminodiacetic acid (HIDA) scan with cholecystokinin (CCK) infusion has been proposed as a method for identifying patients with acalculous cholecystitis who would benefit from LC by quantifying gallbladder ejection fraction (3). In this procedure, ⁹⁹Tc is injected into the patient, the gallbladder is scanned, and then an infusion of CCK is begun, causing the gallbladder to contract and empty. Nuclear medicine images are reviewed before and after CCK infusion, and the gallbladder ejection fraction is calculated as a percentage of the clearance of the isotope. At the time of CCK injection note is also made of exacerbation of symptoms, which if present supports the theory that abnormal contraction and emptying of the gallbladder are responsible for the patient's symptoms. Patients with abnormal gallbladder ejection function (<30% to 40%) would be considered to have poorly function-

ing gallbladders and, therefore, potentially would be cured by cholecystectomy. This retrospective study reviews our experience with acalculous gallbladder disease.

METHODS

From December 1991 to February 1997, 4480 patients underwent cholecystectomy at Baylor University Medical Center. A HIDA scan was performed on 72 patients, who then underwent LC for acalculous gallbladder disease. Records were reviewed for patient age, sex, preoperative symptoms, laboratory and radiographic examination results, operative findings, pathology reports, and patient outcome. The diagnosis of acalculous gallbladder disease was made by history and physical examination findings consistent with biliary tract disease, along with the absence of gallstones or sludge by sonography and failure of other diagnostic measures to diagnose the etiology of symptoms.

Two different methods of administering CCK during the HIDA scan were used. Depending on the preference of the consulting surgeon and the attending radiologist, 20 ng/kg of CCK was infused over 45 minutes (slow technique) or 10 ng/kg of CCK was infused over 5 minutes (fast technique). All patients were informed of the start of the CCK infusion and were asked to report their symptoms. The fast technique was used in an effort to increase the sensitivity of the HIDA scan.

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Two independent interviewers administered a standardized questionnaire. Patients were asked to subjectively grade their symptoms as completely resolved, markedly better, somewhat improved, unchanged, or worse. Responses were then compared with preoperative HIDA scan results, including ejection fraction and/or exacerbation of symptoms with CCK infusion, as well as initial presenting symptoms and results from pathologic examination of the removed gallbladder. Patients who were markedly better after surgery or experienced complete relief of symptoms were reported as having excellent outcomes. Statistical analysis of the data was carried out using a 2-sided Fisher's exact test to detect a difference of the means of each set of data with $P < 0.05$ indicating a significant difference.

RESULTS

Follow-up information was obtained in 59 of 72 patients (82%). Length of time after LC ranged from 15 months to 5 years, with an average of 2.9 years. There were 44 women and 15 men with an average age of 43 years (range, 17 to 86 years). Overall, 48 of 59 patients (82%) had an excellent (completely resolved or markedly better) outcome after LC. Eight patients (14%) were markedly better, and 9 (15%) had minimal or no change. There were 2 treatment failures (symptoms worse). No significant difference in outcome between male and female patients was noted, and patient age did not significantly affect outcome.

Of the 59 patients available for follow-up, 55 were given CCK during their HIDA scan to measure gallbladder ejection fraction and to assess symptom recurrence with CCK injection. A conservative figure of 30% was used as the lower limit of normal gallbladder ejection fraction. Twenty-two patients had abnormal gallbladder ejection fractions ($<30\%$), and 33 patients had normal ejection fractions ($>30\%$). Nineteen of the 22 patients (86%) with an ejection fraction $<30\%$ had excellent outcomes compared with 25 of 33 patients (76%) who had an ejection fraction $>30\%$ ($P = 0.29$).

In addition, outcome data were analyzed using 35% as a cutoff for an abnormal HIDA scan ejection fraction. Twenty-two of the 26 patients (84%) with an ejection fraction $<35\%$ had excellent outcomes compared with 22 of 29 patients (76%) who had an ejection fraction $>35\%$, a finding which was not significant. Data were also analyzed for an ejection fraction cutoff of 40%, and this was not significant.

The return of symptoms after CCK infusion during a HIDA scan was also recorded. Twenty-four of 32 patients (75%) who had exacerbation of symptoms with CCK injection had an excellent result following LC as compared with 20 of 23 patients (87%) without exacerbation of symptoms following CCK infusion ($P = 0.33$).

There were 2 different methods of infusing CCK during a HIDA scan. Of the 32 patients who experienced symptoms with CCK injection, 25 had the slow technique and 7 had the fast technique. Nineteen of the 25 patients (76%) receiving the slow technique had an excellent response, and 5 of the 7 patients (71%) receiving the fast technique had an excellent response ($P = 0.67$).

The primary complaint of each patient was recorded. Right upper quadrant pain was present in 38 of 59 patients (64%), while epigastric pain was present in 15 patients (25%) and either nau-

sea and vomiting or postprandial pain was present in the remaining 6 patients (10%). Thirty of the 38 patients (79%) with right upper quadrant pain had an excellent outcome compared with all 15 patients (100%) with epigastric pain and 3 of the 6 patients (50%) with other chief presenting complaints ($P = 0.25$).

A mixture of pathologic diagnoses was present, with several patients having >1 histopathologic diagnosis. The most common diagnosis, chronic cholecystitis, was present in 29 patients (49%), with 12 of these patients also having cholesterosis. Minimal pathologic changes were present in 13 patients (22%), no histopathologic diagnosis was present in 9 patients (15%), and combined acute and chronic cholecystitis was present in 4 patients (7%). Incidental gallstones were not detected in any patient. Given the mixture of histopathologic diagnoses without an obvious trend in outcome, no statistical analysis was performed. In the 22 patients with minimal pathological changes or no histopathologic diagnosis, 18 patients (82%) reported an excellent result.

Preoperative workup of these patients was very thorough, with all 59 patients having sonograms and HIDA scans. Additionally, 23 patients had documented computed tomography scans, 11 patients had upper gastrointestinal contrast studies, 11 patients had esophagogastroduodenoscopy, 7 patients had colonoscopy, 5 patients had endoscopic retrograde cholangiopancreatography, and 3 patients had barium enemas.

A total of 6 patients had a preoperative diagnosis of irritable bowel disease, and 5 patients were diagnosed with irritable bowel disease after LC. Their outcomes were similar to those of the rest of the study group. Seven of the 11 patients (63%) had complete resolution of their symptoms, 1 patient felt markedly better, 1 felt somewhat improved, 1 felt unchanged, and 1 felt worse.

DISCUSSION

LC is an effective treatment for biliary tract disease related to gallstones, with resolution of symptoms obtained in approximately 95% of patients (2). The reported resolution of symptoms following cholecystectomy for acalculous gallbladder disease is likewise high, ranging from 82% to 100% (4–14). Even with these excellent results, some authors suggest performing cholecystectomy for acalculous disease only when HIDA scans with CCK infusion demonstrate an abnormally low ejection fraction (30% to 50%) and/or recurrence of symptoms with CCK infusion (5–7, 9, 11, 12). Others have evaluated the usefulness of HIDA scans with CCK and found that they were not accurate predictors of patient outcome (4, 10). All agree that the diagnosis is difficult to make and requires a thorough search for other etiologies of the patient's complaints prior to proceeding with cholecystectomy.

In our study, 72 patients who had acalculous gallbladder disease, underwent HIDA scans with CCK infusion, and were subsequently treated with LC were evaluated, with complete follow-up in 59 patients. The overall response to LC is in agreement with several prior studies; 82% had either markedly improved symptoms or complete relief of symptoms.

Differences in this study compared with others are the wide range of ejection fractions measured prior to LC (0% to 97%) and the inability of the HIDA scan with CCK infusion to accurately differentiate which patients would experience excellent

outcomes from their surgery vs those who would derive little or no benefit from LC. Patients with normal gallbladder ejection fractions (>30%) had the same outcome as those with abnormal gallbladder ejection fractions (<30%). The surgeons in this report have traditionally used a conservative ejection fraction cutoff of 30% to help determine patients who have poorly functioning gallbladders and who would potentially benefit from LC. However, an abnormal ejection fraction <35% or <40% also did not help predict which patients would benefit from LC.

In addition, exacerbation of symptoms during injection of CCK did not accurately predict resolution of symptoms after LC. This result was not affected by the method of CCK infusion. In several studies, pain with CCK infusion has been used prior to proceeding to LC (4, 5, 7, 10). However, several authors have also noted that reproducible symptoms after CCK injection are not a reliable predictor of excellent outcome following LC (4, 10). In the present study, 7 patients had a fast bolus injection of CCK instead of a slow continuous infusion of CCK. Return of symptoms after this bolus injection was not significantly different at predicting improved outcome when compared with the slower CCK infusion.

Since its introduction by Krishnamurthy, the HIDA scan with CCK has been touted as the diagnostic procedure of choice in the group of patients with acalculous gallbladder disease (3). Clearly, the HIDA scan provides physiologic and anatomic information about biliary excretion. In this study if only those patients with abnormal ejection fractions and reproducible symptoms with CCK injection were analyzed, the HIDA scan would seem to be a good predictor for excellent outcomes after LC. However, this study represents one of the largest series of patients with normal HIDA scans who underwent LC. Surprisingly, a normal HIDA scan did not predict a lower success rate for LC.

As technology advances and the indications for LC broaden, there is still no accurate test to predict which patients with presumed acalculous gallbladder disease will benefit from LC (15). When an exhaustive workup in a patient with signs and symptoms consistent with acalculous gallbladder disease is negative,

clinical acumen remains the only reliable test to determine those patients who will benefit from LC.

1. Reddick EJ, Olsen DO. Laparoscopic laser cholecystectomy. A comparison with mini-lap cholecystectomy. *Surg Endosc* 1989;3:131-133.
2. Cameron JC. *Current Surgical Therapy*, 6th ed. St. Louis: Mosby, 1998:404.
3. Krishnamurthy GT, Bobba VR, Kingston E. Radionuclide ejection fraction: a technique for quantitative analysis of motor function of the human gallbladder. *Gastroenterology* 1981;80:482-490.
4. Frassinelli P, Werner M, Reed JF III, Scagliotti C. Laparoscopic cholecystectomy alleviates pain in patients with acalculous biliary disease. *Surg Laparosc Endosc* 1998;8:30-34.
5. Canfield AJ, Hetz SP, Schriver JP, Servis HT, Hovenga TL, Cirangle PT, Burlingame BS. Biliary dyskinesia: a study of more than 200 patients and review of the literature. *J Gastrointest Surg* 1998;2:443-448.
6. Goncalves RM, Harris JA, Rivera DE. Biliary dyskinesia: natural history and surgical results. *Am Surg* 1998;64:493-498.
7. Skipper KK, Sligh SP, Dunn EL, Schwartz AG. Laparoscopic cholecystectomy for an abnormal HIDA scan—a worthwhile procedure. *Dallas Medical Journal* 1998;84:272-274.
8. Misra DC Jr, Blossom GB, Fink-Bennett D, Glover JL. Results of surgical therapy for biliary dyskinesia. *Arch Surg* 1991;126:957-960.
9. Barron LG, Rubio PA. Importance of accurate preoperative diagnosis and role of advanced laparoscopic cholecystectomy in relieving chronic acalculous cholecystitis. *J Laparoendosc Surg* 1995;5:357-361.
10. Jones DB, Soper NJ, Brewer JD, Quasebarth MA, Swanson PE, Strasberg SM, Brunt LM. Chronic acalculous cholecystitis: laparoscopic treatment. *Surg Laparosc Endosc* 1996;6:114-122.
11. Sorenson MK, Fancher S, Lang NP, Eidt JF, Broadwater JR. Abnormal gallbladder nuclear ejection fraction predicts success of cholecystectomy in patients with biliary dyskinesia. *Am J Surg* 1993;166:672-675.
12. Zech ER, Simmons LB, Kendrick RR, Soballe PW, Olcese JA, Goff WB, Lawrence DP, DeWeese RA. Cholecystokinin enhanced hepatobiliary scanning with ejection fraction calculation as an indicator of disease of the gallbladder. *Surg Gynecol Obstet* 1991;172:21-24.
13. Reed DN Jr, Fernandez M, Hicks RD. Kinevac-assisted cholescintigraphy as an accurate predictor of chronic acalculous gallbladder disease and the likelihood of symptom relief with cholecystectomy. *Am Surg* 1993;59:273-277.
14. Smith A, Chapman C, Cunningham P. The utility of the CCK DISIDA scan in the treatment of occult biliary tract disease. *Am Surg* 1995;61:220-225.
15. Johanning JM, Gruenberg JC. The changing face of cholecystectomy. *Am Surg* 1998;64:643-648.