

# Hyperkinetic Gallbladder: An Indication for Cholecystectomy?

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**Cholecystectomy may benefit children with biliary colic without stones on ultrasound (US) or low ejection fraction on cholecystokinin-hepatobiliary iminodiacetic acid (CCK-HIDA) scan. Children with symptomatic biliary colic and abnormal HIDA scan, specifically those with high ejection fractions, may benefit from cholecystectomy. All patients younger than 18 years old undergoing cholecystectomy from 2008 to 2012 in our practice were reviewed. Patients with a negative US and CCK-HIDA ejection fractions 80 per cent or greater were included in the study. Patient data were extracted from charts, whereas postoperative symptoms were obtained by phone interviews. Of 174 patients who underwent cholecystectomy, 12 (7%) met study criteria. All patients (12 of 12) had evidence of cholecystitis on the final pathology note. All 11 patients contacted had relief of colic after gallbladder removal with a mean follow-up of 16 months. A subset of pediatric patients with high ejection fractions on CCK-HIDA and symptomatic biliary colic may have symptomatic relief with cholecystectomy.**

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**T**HE MANAGEMENT OF right upper abdominal pain in the pediatric patient free from stones on ultrasound (US) is a challenge. Hepatobiliary iminodiacetic acid (HIDA) scan supports the diagnosis of biliary dyskinesia when nuclear activity over the gallbladder decreases 35 per cent or less after administration of cholecystokinin (CCK). This measurement, termed ejection fraction (EF), has a 70 to 90 per cent sensitivity in predicting resolution of symptoms with cholecystectomy in pediatric patients with the lower EF values having greater predicted symptom resolution.<sup>1, 2</sup> Recent studies show that patients who exhibit pain during CCK injection as part of the HIDA examination (CCK-HIDA), regardless of EF, appear to have relief of pain after cholecystectomy.<sup>3-5</sup>

We wished to refine the use of CCK-HIDA by reviewing patients who had a vigorous emptying of the gallbladder in response to the standard dose of CCK during a CCK-HIDA examination and thus a high EF value. We hypothesized that symptomatic biliary colic, plus a high EF value, would be especially predictive of pain relief after cholecystectomy. Patients with

such a “hyperkinetic gallbladder” may be a subset of patient who might have a particular benefit from cholecystectomy.

## Methods

Patients undergoing cholecystectomy during a 4-year period between January 2008 and December 2011 were reviewed, including final reports for all radiological (principally US) and nuclear medicine studies (CCK-HIDA). Positive US included gallstones, gallbladder wall thickening, sludge, or polyps. Patients with normal gallbladders on US were then evaluated by CCK-HIDA. EF 80 per cent or greater was arbitrarily set as a threshold for inclusion in the study.

Demographic and clinical indices of interest included sex, age, body mass index (BMI), family history, and associated medical conditions. Diagnostic information included laboratory values, US, HIDA scan results including EF and reproduction of pain with CCK administration, additional imaging study results, operative report, and pathology. The patients’ pre- and postoperative course was reviewed from their inpatient and outpatient medical records and in phone interviews by a single coauthor to determine resolution of symptoms.

Descriptive summary data were used so no statistical analysis was conducted.

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## Results

Over 4 years reviewed, there were 174 patients who underwent cholecystectomy: 80 (46%) with positive US examinations and the remainder undergoing CCK-HIDA. Twelve (7%) had a negative US and CCK-HIDA with an EF 80 per cent or greater and constituted the study group. There were four (33%) females and eight (66%) males with a mean age of 13.4 years (range, 7 to 17 years). The mean BMI was 24.8 kg/m<sup>2</sup> (range, 16.1 to 36.6 kg/m<sup>2</sup>). Five (42%) had at least one immediate family member who had undergone cholecystectomy. One-third (four of 12) had comorbid conditions, including diabetes mellitus (one), asthma (four), hypothyroidism (one), and gastroesophageal reflux (one).

Preoperatively all had pain in either right upper quadrant (10) or epigastrium (two). The pain was specifically described as postprandial in five patients. Three-fourths (eight of 12) had daily bouts of nausea or emesis. The symptoms were chronic in all with symptoms persisting for at least 3 months.

Laboratory values were within normal limits in 11 of 12 patients. One patient had a serum total bilirubin of 2.4 mg/dL (normal less than 1.3 mg/dL) with normal liver enzyme levels. Although free from gallbladder pathology on US, the examination found changes consistent with fatty liver in two patients (17%). EF exceeded 80 per cent in all, with a mean of 88 per cent, range 82 to 98 per cent, and median 91 per cent. Mean CCK pain score was 4.5 (range, 0 to 10; median, 5).

Patients had undergone a number of additional studies: esophagoduodenoscopy (EGD [nine]), computed tomography of the abdomen (two), upper gastrointestinal series (two), and colonoscopy (one). EGD examinations were normal in five patients. Four had evidence of esophageal or gastric pathology: eosinophilia (one), mild gastritis (two), and hiatal hernia (one). Proceeding with cholecystectomy as the primary intervention, as opposed to addressing other abdominal pathology, was a joint decision made by both the surgeon and gastroenterologist.

All procedures were laparoscopic cholecystectomies performed without complications. Final pathological examination revealed chronic cholecystitis in all patients (12 of 12 [100%]) and cholesterolosis in one-fourth (three of 12). Telephone contact was made with parents of 11 patients. All were free from pain and gastrointestinal symptoms at 3 to 45 months (mean follow-up of 16 months). All parents reported an improvement in their children's quality of life.

## Discussion

We found a subset of 12 patients without gallstones but with biliary colic and EF 80 per cent or greater on CCK-HIDA who were treated successfully with

cholecystectomy. Relief of their symptoms suggests another pathological manifestation of abnormal gallbladder function, one characterized by vigorous contraction of the gallbladder in response to CCK provocation that produces abdominal pain. Biliary dyskinesia, traditionally defined as biliary pain on CCK-HIDA and a low EF of 35 per cent or less,<sup>6</sup> may be a more general phenomenon that includes abnormally high EF as well. Emergence of a new classification of biliary pathology is not surprising given the recent overall increase in biliary pathology leading to cholecystectomy, now at 1.5 to 4 per cent in the pediatric age group,<sup>7</sup> many from biliary dyskinesia.<sup>8,9</sup> The indications for cholecystectomy for biliary dyskinesia have undergone basic modifications, a reflection of the difficulty in defining the condition and its response to surgery. A recent study of 200 pediatric patients used EF 40 per cent or less rather than the traditional threshold of 35 per cent or less.<sup>10</sup> Even with this more liberal criterion, symptoms completely resolved in 23 of 28 (79%) patients with pathological evidence of chronic cholecystitis in 21 of 28 (72%). More recent studies suggest that pain with CCK provocation during CCK-HIDA is the primary predictor of relief of abdominal pain after surgery.<sup>3,11</sup> Morris-Stiff and coworkers<sup>3</sup> noted that 42 patients who experienced recreation of biliary pain when given CCK as part of a CCK-HIDA examination all had resolution of pain after cholecystectomy, including 25 who had EF greater than the 35 per cent threshold that was held diagnostic for biliary dyskinesia. Moreover, the specimens in 41 of the 42 showed evidence of chronic cholecystitis. Their experience mirrors our own results.

Complicating the diagnosis of biliary dyskinesia is the failure to provide an etiology or clear pathophysiology of how CCK provocation causes biliary pain. Theories include abnormal motility as a result of decreased or dysfunctional CCK receptor sensitivity, decreased smooth muscle motility, and decreased ejection fraction.<sup>12-14</sup> Careful pathological examination of gallbladders from patients with biliary dyskinesia demonstrates increased numbers of mast cells in the muscularis of unknown significance.<sup>15</sup>

Our experience, admittedly limited, suggests that there is pathological responses of an overly vigorous response to CCK, leading to painful contraction of the gallbladder. All had pathological evidence of chronic cholecystitis and all had resolution of symptoms after removal of the gallbladder. In view of the 80 per cent success rate in patients with biliary dyskinesia using the low EF threshold of 35 per cent or less or 40 per cent or less, our experience with pain relief among patients with EF 80 per cent or greater indicates that using the high threshold will have an equivalent salutary effect.

The efficacy and safety of pediatric laparoscopic cholecystectomy has drawn interest because of the increasing numbers of children undergoing the procedure.<sup>16, 17</sup> Operative complication rates of 0.3 to 2 per cent are comparable to those observed in adults, the most common including superficial wound infection, ileus, and postoperative pain. Potential risks of major ductal injuries must be weighed against the many missed school days and parents' work days that are familiar to pediatricians, gastroenterologists, and surgeons.

The limitation of this study is the small sample size and selection bias in the inclusion of only patients who underwent cholecystectomy. A prospective study of patients with elevated EF on HIDA who did not undergo cholecystectomy likely will require multiple centers. Until such a study can be carried out, carefully selected patients with EF 80 per cent or greater and symptomatic biliary colic may benefit from cholecystectomy. Parents need to be informed of the lack of definite causal links between the child's symptomatology and the results of US and CCK-HIDA.

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