



Is hyperkinetic gallbladder an indication for cholecystectomy?

Shireesh Saurabh¹ · Benjamin Green¹

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Abstract

Background The (99m) technetium-labelled hepato imino diacetic acid (HIDA) scan is widely used to evaluate patients with biliary colic with a normal trans-abdominal ultrasound scan. Most studies recommend cholecystectomy for patients with biliary dyskinesia, defined by gallbladder ejection fraction (GBEF) of less than 35–40% on HIDA scan. There are no recommendations regarding management of hyperkinetic gallbladder defined by GBEF of greater than 80% on HIDA scan. The aim of our study was to evaluate the outcomes following cholecystectomy on patients with biliary colic associated with hyperkinetic gallbladder.

Methods We performed a retrospective chart review of all patients with biliary colic associated with hyperkinetic gallbladder that underwent cholecystectomy in our practice from July 2014 to February 2018. Data collection included age, gender, body mass index, preoperative symptoms, comorbidities, additional tests, ejection fraction, surgery, and histopathology of the gallbladder. Symptomatic improvement was assessed during routine 2-week postoperative visit and a follow-up phone interview.

Results Thirty-two patients had undergone laparoscopic cholecystectomy during the study period for symptomatic hyperkinetic gallbladder. All the patients had abdominal pain related to food intake and 17 (53%) patients had worsening of symptoms with CCK infusion. The average GBEF was 92%. Chronic cholecystitis was seen in 29 (90%) patients on pathology. 23 (74%) patients had complete resolution of biliary symptoms, 5 (16%) had improved symptoms, and 3 (10%) had no change in symptoms.

Conclusion Patients with biliary colic and hyperkinetic gallbladder respond favorably to laparoscopic cholecystectomy. Our results suggest that patients with biliary colic in the setting of hyperkinetic gallbladder have symptomatic improvement following cholecystectomy.

Keywords Hyperkinetic gallbladder · Ejection fraction · CCK-HIDA scan · Laparoscopic cholecystectomy · Chronic cholecystitis

Hyperkinetic gallbladder has been previously described in the literature; however, it is not a very well-understood condition. It is thought to arise due to rapid contraction and emptying of the gallbladder. Cholecystokinin 99m technetium-labelled hepato imino diacetic acid (CCK-HIDA) scan is used to diagnose hyperkinetic gallbladder. Ejection fraction of 80% or more is commonly used to define hyperkinetic gallbladder [1–4]. Biliary dyskinesia is a more commonly studied gallbladder functional disorder. It is diagnosed by an ejection fraction of less than 35% on CCK-HIDA scan. Most

studies show a favorable symptom response to cholecystectomy [5–9]. There are not enough data available regarding management of patients with symptoms of biliary colic along with gallbladder hyperkinesia demonstrated on CCK-HIDA scan in the absence of cholelithiasis. The purpose of this study was to evaluate the response of patients with biliary colic and hyperkinetic gallbladder to cholecystectomy.

Materials and methods

A retrospective chart review of all the patients undergoing cholecystectomy in our practice from July 2014 to February 2018 was performed. Patients with food related abdominal pain, normal gallbladder US, and ejection fraction of

✉ Shireesh Saurabh
shireesh22@gmail.com

¹ General/Bariatric Surgery, Mercy Hospital, 540 East Jefferson Street, Suite 205, Iowa City, IA 52245, USA

80% or greater on CCK-HIDA scan were included in the study. Patients with abnormal US as evidenced by presence of cholelithiasis, pericholecystic fluid, gallbladder wall thickening, polyps, or sludge were excluded from the study. Outpatient clinic notes and hospital notes were used to collect the data. The study was approved by Mercy Iowa City Institutional Review Board (IRB), and data acquisition and storage was in compliance with IRB's guidelines.

The information collection included age, gender, body mass index (BMI), preoperative symptoms, comorbidities, additional tests performed other than US and CCK-HIDA scan, gallbladder ejection fraction, surgery type (laparoscopic or open), length of hospital stay, 30-day postoperative readmission, and histopathology of the gallbladder. Intraoperative gallbladder appearance information was collected by reviewing the operative report and pictures taken during surgery.

Early 2-week postoperative visit data were collected by reviewing the clinic notes. Long-term follow-up data were collected through telephone interview using a standardized questionnaire. Patients were asked if they had a complete resolution, partial resolution, no change, or worsening of symptoms following cholecystectomy. Data were recorded as a descriptive statistics and calculated as mean \pm standard deviation along with range.

Results

A total of 32 patients met the inclusion criteria and were included in the study. Among these patients, 31 (97%) were available for long-term follow-up through telephone interview. All surgeries were performed at Mercy Hospital, Iowa City by 2 surgeons. All the surgeries were completed laparoscopically without any intraoperative complications. All the patients were discharged home the same day of surgery and there were no postoperative 30-day readmission or reoperation.

The mean age was 46 ± 12.0 years (range 21–64), BMI average was 30 ± 6.50 (range 18.8–41.9), and the majority of patients ($n = 27$, 84%) included in the study were women. All patients had negative gallbladder US. CCK-HIDA scan was performed in all the patients included in the study and the mean gallbladder ejection fraction was $92\% \pm 0.05$ (range 82–99%). Reproduction of symptoms following CCK administration was seen in 20 (62.5%) patients. In addition to US and HIDA scan, 22 (68.7%) patients also underwent additional tests like esophagogastroduodenoscopy (EGD), colonoscopy, computed tomography (CT) scan, gastric emptying study, and upper gastrointestinal contrast study. Most common medical problem seen in these patients was gastroesophageal reflux disease (GERD) and was documented in 22 (68.7%) patients past medical history.

Pathology results were available for all the patients. The most common pathological finding seen was chronic cholecystitis in 29 (90.6%) patients. Two patients had gallbladder with no pathological abnormality. Cholesterosis as a sole pathological finding was seen in only one patient. 21 (91.3%) patients with complete resolution of symptoms with cholecystectomy had chronic cholecystitis on pathology. 1 had cholesterosis and 1 had no abnormality. Out of five patients with partial resolution of symptoms, 4 had chronic cholecystitis and 1 was normal gallbladder. All three patients with no change in symptoms with cholecystectomy had chronic cholecystitis on pathology.

Two-week postoperative evaluation included 32 patients. At the 2-week outpatient postoperative visit, 24 (75%) patients had complete resolution of symptoms. Partial resolution of symptoms was seen in 5 (15.6%) patients and 3 (9.4%) patients had no change in symptoms. No patient had worsening of symptoms. Telephone contact was made with 31 patients and the average follow-up duration was 12 (range 2–33) months. 23 (74.2%) patients had complete resolution of symptoms, 5 (16.2%) patients had partial resolution of symptoms, and 3 (9.6%) patients had no change in symptoms (Fig. 1). The three response groups had similar demographic profile, preoperative symptoms, and CCK-HIDA scan findings (Table 1). Reproduction of symptoms following CCK administration was seen in 19 (61%) patients. 13 of these patients had complete resolution of symptoms and 3 had partial resolution of symptoms. Three patients had no change in symptoms. 84% of patients who had reproduction of symptoms with CCK administration had partial or complete resolution of symptoms with cholecystectomy (Fig. 2).

Intraoperative gallbladder appearance was documented in all 32 patients. In the complete response group, 11 (45.8%) patients had omental adhesions to the anterior surface of the gallbladder, 4 (16.7%) patients had periduodenal adhesions to the infundibulum of the gallbladder, 2 (8.3%) patients had thickened gallbladder wall, and 7 (29.2%) patients had normal looking gallbladder. In the

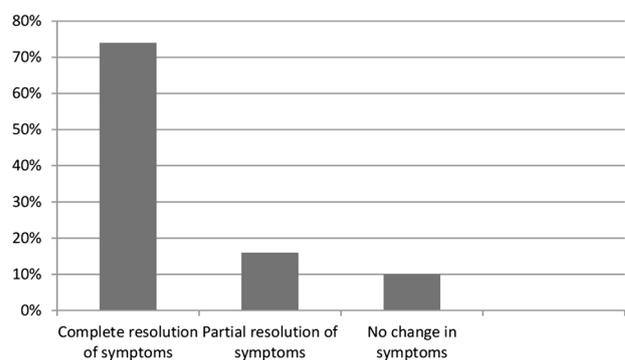
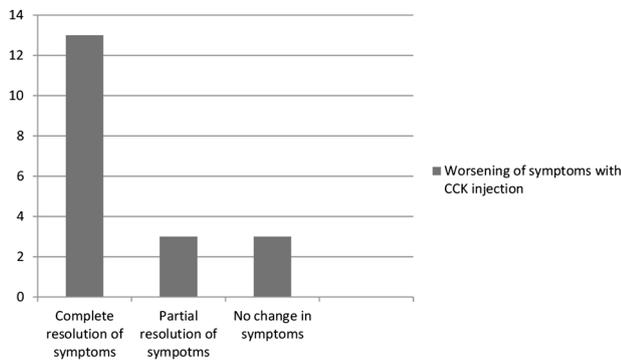


Fig. 1 Demonstrates degree of relieve of preoperative symptoms after laparoscopic cholecystectomy

Table 1 Demonstrates comparison between patients with different long-term responses to cholecystectomy

	Complete resolution of symptoms	Partial resolution of symptoms	No change in symptoms	Worsening of symptoms
Number of patients (<i>n</i> = 31)	23 (74.2%)	5 (16.2%)	3 (9.6%)	0
Average age (years)	45.7 ± 12.8 (21–64)	42.4 ± 8.08 (35–56)	54.7 ± 7.02 (48–62)	0
Gender—female/male	18/5	5/0	3/0	0
Average BMI (kg/m ²)	30.3 ± 6.05 (18–40.3)	32 ± 8.92 (41.9–19.8)	24.7 ± 4.55 (21.6–29.9)	0
Abdominal pain related to food	23 (100%)	5 (100%)	3 (100%)	0
Reproduction of symptoms with CCK	13	3	3	0
Average ejection fraction	91.6% ± 0.06 (82–99%)	94% ± 0.04 (89–99%)	92.7% ± 0.01 (91–94%)	0
Chronic cholecystitis on pathology	21 (91.3%)	4 (80%)	2 (100%)	0

**Fig. 2** Demonstrates preoperative reproduction of symptoms with cholecystokinin (CCK) injection

partial response group, 3 (60%) patients had omental adhesions to the anterior surface of the gallbladder, 1 (20%) had thickened gallbladder, and 1 (20%) had normal looking gallbladder. All 3 (100%) patients in the no-response group had omental adhesions to the anterior surface of the gallbladder wall (Table 2). Out of the seven normal looking gallbladder, 5 (71%) had chronic cholecystitis on pathology and 2 (29%) had no pathological abnormality.

Discussion

Cholecystokinin (CCK) is a polypeptide secreted by duodenal mucosa in response to ingestion of fats and amino acids. It induces contraction of the gallbladder, relaxation of the sphincter of oddi, and lower esophageal sphincter. It also increases secretion of hepatic bile and pancreatic enzymes [10, 11].

The pathophysiology of gallbladder hyperkinesia causing biliary colic is not very clear. One of the possible explanations could be that these patients have increased density of cholecystokinin receptors or increased secretion of CCK, which causes the gallbladder to contract intensely to fatty food ingestion, resulting in abdominal pain. Rapid emptying of the gallbladder could also lead to increased intraluminal pressure. This increased gallbladder pressure could cause mucosal injury and chronic inflammation as seen on histopathology [12]. In our study, chronic cholecystitis was found on histological evaluation of 90% of the gallbladders, indicative of long standing mucosal inflammation. Similar findings were reported by Lindholm et al. and their study showed all 12 patients (100%) to have chronic cholecystitis on final pathological examination of the gallbladder [1]. CCK levels were not measured in our study or in any study related to gallbladder hyperkinesia. Future studies looking into CCK levels might be able to provide more insight into the pathophysiology of gallbladder hyperkinesia.

Table 2 Comparison of intraoperative gallbladder appearance and response rates following cholecystectomy

Intraoperative gallbladder appearance	Complete resolution of symptoms (24)	Partial resolution of symptoms (5)	No change in symptoms (3)
Omental adhesions to anterior surface of gallbladder	11 (45.8%)	3 (60%)	3 (100%)
Periduodenal adhesions to infundibulum of gallbladder	4 (16.7%)	0	0
Thickened gallbladder wall	2 (8.3%)	1 (20%)	0
Normal looking gallbladder	7 (29.2%)	1 (20%)	0

Most of the patients with hyperkinetic gallbladder do not get referred to surgeons for cholecystectomy as HIDA scan read mostly focuses on low gallbladder ejection fraction. They undergo multiple additional tests, and in our study 68.7% patients had undergone additional studies other than US and CCK-HIDA scan before cholecystectomy.

In the present study, 74% of patients experienced complete and 16% experienced partial resolution of preoperative abdominal symptoms after laparoscopic cholecystectomy. These findings are consistent with those reported by Holes-Lewis et al. who reported 79% patients to have complete resolution of symptoms and 97% of patients to have symptomatic improvement with cholecystectomy [3]. Similarly, Law et al. reported a 69.3% symptom response to cholecystectomy in patients with hyperkinetic gallbladder [2]. In pediatric population, Lindholm et al. reported all 11 (100%) patients to have complete resolution of biliary colic symptoms after laparoscopic cholecystectomy [1].

In a study performed by DuCoin et al., almost 90% patients with biliary colic, GBEF > 35% and symptoms reproducible with CCK injections had a complete resolution of symptoms with cholecystectomy [13]. Another study by Morris-Stiff shows that reproduction of symptoms with CCK injection is superior to ejection fraction measurement in predicting resolution of symptoms after cholecystectomy in patients with biliary dyskinesia [14]. In our study, 61% patients had reproduction of symptoms by CCK injection. 84% of these patients had complete or partial resolution of symptoms with cholecystectomy.

Intraoperative appearance of gallbladder was not indicative of response to cholecystectomy. In the complete response group, 29% patients had normal looking gallbladder, while in the no-response group all patients had omental adhesions to the anterior surface of the gallbladder. This underscores the point that it is a functional problem of the gallbladder and not anatomical.

The response rate to cholecystectomy in the present study is comparable to the historic response rate seen in patients who undergo cholecystectomy for symptomatic cholelithiasis [15–18]. Bates et al. evaluated the response of cholecystectomy on 292 patients with symptomatic cholelithiasis and 34% patients had persistent abdominal pain 1 year after surgery [15]. McMahan et al. evaluated symptoms outcome 1 year after laparoscopic and minilaparotomy cholecystectomy for symptomatic cholelithiasis and found 90% patients to have symptoms improvement [16].

One of the strength of our study was the long-term follow-up through telephone interview. We were able to obtain long-term follow-up in 97% of the patients who had cholecystectomy for symptomatic hyperkinetic gallbladder. The average follow-up duration was 12 months. Telephone interview helped us in assessing symptom response by directly talking to the patients and not depending on only

clinic notes. To our best knowledge, this is the largest study evaluating the response to cholecystectomy in these patients.

The limitations of this study are small sample size, retrospective study design, and a possible selection bias in including only patients with hyperkinetic gallbladder who underwent cholecystectomy. Future studies could include patients undergoing cholecystectomy for biliary dyskinesia or symptomatic cholelithiasis as a control group.

Conclusion

In this retrospective study, 90% patients with biliary colic symptoms and hyperkinetic gallbladder on HIDA scan had complete or partial resolution of symptoms with cholecystectomy. These findings are significant and promising; however, large, well-designed, prospective studies will be required to confirm these results.

Compliance with ethical standards

Disclosures Drs. Shireesh Saurabh and Benjamin Green have no conflicts of interest or financial ties to disclose.

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