



# Abnormal pathology in cholecystectomy patients with normal preoperative studies

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**Background:** Right upper quadrant abdominal pain is a common complaint often associated with gallbladder disease. However, there may be a subset of patients with true gallbladder pathology who do not have definitively positive preoperative studies. We seek to demonstrate the outcomes in this patient subpopulation.

**Methods:** A retrospective chart review of all patients undergoing laparoscopic cholecystectomy for clinical history of biliary symptoms with classically “normal” ultrasound and HIDA scan were included. Patients were polled regarding their symptoms preoperatively and postoperatively at time of surgical follow-up.

**Results:** Thirty-three patients underwent minimally invasive cholecystectomy during the study period with normal preoperative evaluations despite clinical symptoms consistent with biliary pathology. Of these 33 patients, all reported resolution or significant improvement in symptoms post-operatively.

**Conclusions:** Currently available methods for the preoperative evaluation of gallbladder pathology may underdiagnose the true incidence of gallbladder disease, and cholecystectomy should be considered in these patients with a clinically significant history despite normal studies.

**Keywords:** Cholecystectomy; biliary hyperkinesia; HIDA scan; ultrasound

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## Introduction

Biliary dyskinesia and symptomatic gallstones are indications for cholecystectomy (1), but there are patients with RUQ pain, a normal ultrasound and a normal or high GBEF. Patients may not be offered cholecystectomy based on “normal” studies.

There is little literature on patients with biliary symptoms, normal ultrasound, and a normal or high ejection fraction. Beginning with a subset of gastric bypass patients with upper abdominal pain and normal studies who improved symptomatically after cholecystectomy, we found they had abnormal histopathology, calling into question

what is “normal”. We then looked at all patients with symptoms but normal studies.

## Methods

After obtaining approval from the Penn State College of Medicine Institutional Review Board, all patients who underwent cholecystectomy in the Division of Minimally Invasive and Bariatric Surgery at the Hershey Medical Center between July 1, 2007 and December 31, 2013 were evaluated by chart review. Patients found to have an abnormal preoperative ultrasound, including the presence of polyps, gallstones, pericholecystic fluid, or gallbladder

wall thickening were excluded. Patients with a low GBEF, defined as below 35%, were also excluded. A total of 33 patients with biliary symptoms, normal ultrasounds, and reportedly “normal” GBEF (>35%) were identified and studied.

All 33 patients underwent robotic or laparoscopic cholecystectomy on the basis of symptoms that were attributable to the biliary tract, including epigastric or right upper quadrant abdominal pain with or without radiation to the back, and with or without fatty food intolerance. No patients experienced intra- or postoperative complications. Cholecystectomy was performed through a variety of approaches, including 3-port, 4-port, single-incision, and robotic cholecystectomy, according to the operating surgeon’s preference. All patients were seen in follow-up 4 to 6 weeks after surgery and evaluated for symptom resolution.

## Results

The mean GBEF among the included patients was 79.8%, with a range of 36–98%. One patient was excluded from this calculation due to a GBEF reported simply as “brisk” without a numeric value, but presumed to be in the normal range. Pathology reports were reviewed on all patients. Overall, of the 33 patients, 31 (93.9%) had abnormal pathologic findings, with only two specimens read as a normal gallbladder. Thirty patients (90.9%) had histopathologic chronic cholecystitis. Ten patients (30.3%) were found to have cholesterosis, sludge or gallstones despite a negative ultrasound. One patient (3.3%) had a polyp in addition to both stones and chronic cholecystitis, despite a negative ultrasound. Patients with abnormal findings on their surgical pathology report had an average GBEF of 80%. One hundred percent of patients were evaluated post-operatively and reported resolution or significant improvement in their pre-operative symptoms.

## Discussion

Multiple indications exist for elective cholecystectomy, including biliary hypokinesia with a GBEF <35%, as well as other common pathologies such as cholelithiasis and cholecystitis. There is very little available data regarding the upper limit of normal for GBEF. One series of adolescent patients evaluated clinical outcomes following cholecystectomy in patients with a GBEF >80%, which they defined as “hyperkinesia.” All patients in this study who

underwent cholecystectomy with a pre-operative diagnosis of biliary hyperkinesia reported resolution of symptoms at the time of follow-up, and all were found to have chronic cholecystitis on pathology (2). Our series yields similar results, with all patients reporting symptom resolution, and the vast majority having abnormal pathology.

Our findings indicate a potential deficiency in the currently available diagnostic modalities for evaluating gallbladder disease, and perhaps a limitation of current definitions of normal gallbladder function. No discrete value exists for the upper limit of normal GBEF. Our series and others have demonstrated a strong correlation between biliary hyperkinesia and chronic pathologic changes (2-5). In our series of patients with biliary symptoms but normal preoperative studies, cholecystectomy led to symptomatic relief in 100% of patients. In addition, 93.9% of patients had unexpected pathologic findings in the gallbladder despite the lack of radiologic evidence of dysfunction or disease.

Unfortunately, the diagnosis of biliary dyskinesia is controversial and there is little consensus in the literature over the exact protocol for HIDA scan and its interpretation. Cholecystokinin (CCK)—induced provocation of abdominal pain and gastrointestinal symptoms is a poor indicator of functional disorder of the gallbladder, and should not be used to diagnose such conditions (6). Few studies have actually validated their stated normal values (varying from 25–65%) and normal values that are quoted are generally based on small numbers of individuals.

Our institution also does not have an upper limit of normal for GBEF; other institutions will sometimes give an upper limit between 65 and 80%, where a higher value would be read as “hyperkinesia.” There is a small number of studies suggesting that symptomatic patients with a higher than normal GBEF can benefit from cholecystectomy. Huckaby *et al.* reported on three adolescents with GBEFs between 72% and 81%, all of whom experienced improvement in symptoms after cholecystectomy (4). Holes-Lewis *et al.* reported a series of 108 patients with a GBEF of greater than 80%. Of the 108 original patients, 44% underwent cholecystectomy and of these, 97% had complete resolution of symptoms (7). Cook *et al.* performed a similar questionnaire study and found that of 18 patients with a GBEF of greater than 80%, 79% had complete remission of their symptoms and 21% had significant improvement (5).

Our study is limited in that it is a retrospective review.

Assessment of post-operative symptomatology was not performed in a formal manner, and it was obtained by review of clinic documentation at the time of the initial post-operative visit. Long term follow-up was not conducted. Overall, the short-term data from our institution indicates a potential discrepancy between the sensitivity of ultrasound and HIDA scan for the diagnosis of gallbladder disease identified on pathologic evaluation, and correlated to clinical improvement following elective cholecystectomy. A thoughtful interpretation of elevated or “normal” GBEF in the setting of a patient who presents with clinically classic complaints indicative of gallbladder pathology may allow for the judicious use of cholecystectomy to alleviate suffering in this patient population.

### Conclusions

Based on our series of patients, we believe that classic radiologic studies may tend to under-diagnose gallbladder pathology. The majority of symptomatic patients had pathologic findings despite normal preoperative studies and experienced resolution of symptoms after removal of the gallbladder. Even in the absence of pathologic findings, patients with a clinical diagnosis of biliary colic experienced resolution of symptoms following cholecystectomy. We propose that the usual indications for  $\gamma$  should be expanded to include patients with symptoms attributable to the gallbladder despite a normal ultrasound or a normal or elevated GBEF.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest

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to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study obtained approval from the Penn State College of Medicine Institutional Review Board (No. PRAMS044820EM).

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