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RESEARCH ARTICLE

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Biliary Dyskinesia - Is It Real?

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ABSTRACT

Introduction: Biliary dyskinesia is a functional gallbladder disorder characterized by altered gallbladder motility. This often presents as history of biliary symptoms without imaging evidence of gallstones, sludge, or other structural pathology. The diagnosis is made by demonstration of abnormal gallbladder emptying on hepatic iminodiacetic acid analogue scan with cholecystokinin administration (HIDA-CCK). The aim of this study was to determine if patients with biliary dyskinesia who undergo cholecystectomy have abnormal pathology and resolution of symptoms.

Methods: This is a retrospective cohort study reviewing patients with symptomatic cholelithiasis or biliary dyskinesia who underwent cholecystectomy by a single surgical practice from 2015 to 2019. Clinical symptoms, radiologic findings and surgical pathology were assessed. The primary endpoints were pathologic changes and symptom resolution after cholecystectomy. Secondary endpoints were correlation of symptomatic disease with gender, age, and body mass index (BMI). Variables are presented as median (interquartile range [IQR] or frequency [%]).

Results: Four hundred and fifteen patients met inclusion criteria. Of these patients, 89 patients (21%) had biliary dyskinesia. The age of patients with biliary dyskinesia was 46 (33–58) years with the BMI of patients with biliary dyskinesia being 28 (24–33). A total of 82 patients with biliary dyskinesia were women (92%). Patients diagnosed with calculus disease (symptomatic cholelithiasis, acute calculous cholecystitis, choledocholithiasis) had an age of 55 (35–69) years. The majority (214 [66%]) of patients were women with calculus disease and 153 (71%) women had symptomatic cholelithiasis. Significance was observed in BMI between the groups, with the overall being 29 (25–35). The most common presenting symptom was abdominal pain, reported by 86 (97%) patients with biliary dyskinesia. The median ejection fraction (EF) was 18% (11–27%). Three patients with biliary dyskinesia (3%) had a median EF of 94% (86–99%), consistent with hyperkinetic biliary dyskinesia (>80%). Pathology demonstrated chronic cholecystitis in 75 specimens (84%), normal in 9 specimens (10%), and cholesterolosis alone in 5 specimens (7%). All patients experienced resolution of symptoms postoperatively.

Conclusion: Symptomatic patients with evidence of biliary dyskinesia were more likely to be younger and have a lower BMI than those with cholelithiasis and occurred most commonly for women. Most patients with biliary dyskinesia had histologic evidence of chronic gallbladder inflammation. Cholecystectomy resulted in resolution of symptoms in all patients with biliary dyskinesia. Cholecystectomy should be considered for first-line treatment of patients presenting with biliary symptoms, negative ultrasound findings and scintigraphic evidence of abnormal biliary function.

Key Words: Biliary dyskinesia, Cholelithiasis, Ejection fraction, Gallbladder disease, HIDA scan, Laparoscopic cholecystectomy.

INTRODUCTION

Biliary dyskinesia is a functional gallbladder disease without a well-known etiology. Biliary dyskinesia has been linked to obesity and a biliary sphincter of Oddi dysfunction.[1–3] Laparoscopic cholecystectomy has become the standard treatment for symptomatic biliary dyskinesia, but it is a disease that is disproportionately diagnosed in the

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United States.[4] The frequency of biliary dyskinesia has more than doubled between 1991 and 2011 from 43 to 89 per 1,000,000 population in the United States.[4] Norway, Sweden, Australia, and Poland had less than 25 per 1,000,000 in the same time frame.[4] This disparity was even more pronounced in the United States pediatric patients increasing by 700% between 1997 and 2010.[4,5] This disparity and the lack of standard diagnosis until 2016 has led many to believe that biliary dyskinesia is overdiagnosed and that cholecystectomy is overutilized in the United States.[6]

Surgical treatment has proven to be both safe and effective in the treatment of biliary dyskinesia.[7,8] The standard diagnosis criteria, as described by Rome IV in 2016 and originally described by Fink-Bennett et al in 1991, includes the criteria for biliary pain along with no structural pathology and a hepatic iminodiacetic acid analogue scan with cholecystokinin administration (HIDA-CCK) showing an ejection fraction (EF) of less than 40% as well as normal liver enzymes.[9,10] Recent studies have termed this diagnosis as "hypokinetic biliary dyskinesia" and have diagnosed cases of "hyperkinetic biliary dyskinesia" with an EF greater than 80%.[11,12] These studies have shown similar results compared to patients treated with laparoscopic cholecystectomy for hypokinetic biliary dyskinesia.[11,12]

Many studies only show symptom resolution for about 85% of patients with biliary dyskinesia.[6,13–15] HIDA scans have also been questioned in their accuracy, with repeated scans showing inconsistent results.[16,17] Overall this potentially leaves approximately 15% of patients undergoing potentially unnecessary operation management and leaves the need for a more refined diagnostic approach. The aim of this study is to evaluate if patients with biliary dyskinesia have abnormal gallbladder pathology and if their symptoms resolve after cholecystectomy.

METHODS

This is a retrospective cohort study reviewing patients who underwent cholecystectomy by a single surgical practice from 2015 to 2019. This study was reviewed and approved by the Institutional Review Board and deemed it to qualify for exempt status via the Code of Regulations: 45 CFR 46.104 (d) Category (Exempt Category 4). Diagnosis for our cohort followed standard biliary pain diagnosis, including right upper quadrant ultrasound. If patients reported epigastric abdominal pain, a preoperative esophagoduodenoscopy (EGD) was undertaken to rule out the differential diagnosis such as gastritis, peptic ulcer disease and/or *Helicobacter pylori*. If both the ultrasound and EGD were negative, a HIDA scan with EF was undertaken. If liver enzymes were normal and the HIDA scan was abnormal, laparoscopic cholecystectomy was undertaken. Cholecystokinin-cholescintigraphy was undertaken with the administration of an 8.5 mCi dose of technetium-99m Choletec, along with 1,37 mcg of CCK. Sequential imaging was performed over the abdomen for 60 minutes following tracer administration, and at 60 minutes, a 30-minute infusion of CCK was initiated. Additional imaging was conducted for 30 minutes to assess gallbladder emptying and generate a time/activity curve. Patients ≥17 years old who underwent cholecystectomy for symptomatic cholelithiasis, or biliary dyskinesia were included.

Biliary dyskinesia was defined as gallbladder EF <40% or >80% on HIDA-CCK, characterized as hypokinetic and hyperkinetic biliary dyskinesia, respectively. Clinical symptoms, radiologic findings and surgical pathology were evaluated. The primary endpoints were pathologic changes and symptom resolution after cholecystectomy. Secondary endpoints were correlation of symptomatic disease with gender, age, and body mass index (BMI). Variables are presented as median (interquartile range [IQR] or frequency [%]).

RESULTS

Four hundred and thirty-two patients who underwent cholecystectomy were screened and 415 were included for analysis. Seventeen were excluded from analysis due to presenting with gallbladder polyps, which is not a calculus disease of the gallbladder. A total of 326 patients (79%) had calculus disease of the gallbladder diagnosed preoperatively (symptomatic cholelithiasis, acute calculous cholecystitis, choledocholithiasis), whereas 89 patients (21%) had biliary dyskinesia as a preoperative diagnosis. Age of patients with biliary dyskinesia was 46 (33–58) years versus 55 (35–69) years for patients diagnosed with calculus disease ($P = .014$). Gender was found to be statistically significant as 82 (92%) patients with biliary dyskinesia were women and 214 (66%) of those had symptomatic calculus disease ($P < .001$). The overall BMI was 29 (25–35), whereas the BMI for patients with calculus disease versus biliary dyskinesia was 31 (26–36) and 28 (24–33), respectively ($P = .015$) (**Table 1**). Of note, 2 patients were 17 years old. Overall, patients with biliary dyskinesia were significantly more often women, younger, and with a lower BMI when compared to those with a preoperative calculus disease diagnosis.

A total of 17 patients (4%) who underwent cholecystectomy had gallbladder polyps diagnosed preoperatively.

Table 1.
Characteristics of Patients with Calculus Disease or Biliary Dyskinesia Requiring Cholecystectomy

Variable	Total N = 415	Calculus Disease n = 326 (78.3)	Biliary Dyskinesia n = 89 (21.4)	*P*
Age (y), median [IQR]	52 [36–68]	55 [35–69]	46 [33–58]	.014[a]
Gender				<.001[b]
Women (%)	296 (71.3)	214 (65.6)	82 (92.1)	
Men (%)	119 (28.7)	112 (34.4)	7 (7.9)	
BMI, median [IQR]	29 [25–35]	31 [26–36]	28 [24–33]	.015[a]

[a]Mann-Whitney *U* test, percentages in (%) represent columnar group percentages.
[b]Fisher's exact test.

Age of patients with polyps was 58 (50–73) with a BMI of 26 (22–29). Most patients were women (64%).

The top presenting symptoms of biliary dyskinesia were abdominal pain (97%) and nausea (38%) (**Table 2**). Fifty patients (56%) an EGD was undertaken preoperatively. Additionally, all 89 patients underwent a HIDA scan and 86 had an EF < 40% (94%) and 3 patients had hyperkinetic dyskinesia with an EF > 80% (3%) (**Table 3**).

Intraoperatively or postoperatively on the back table, gallstones were seen for 9 patients with biliary dyskinesia (10%). Pathology showed chronic cholecystitis in 75 specimens (83%) and normal or no pathological findings in 9 specimens (10%). Cholesterolosis was found alone in 5 cases (7%) and overall for 24 specimens (27%) (**Table 4**). There was cholelithiasis overall in 16 specimens (18%). All 89 patients experienced resolution of their symptoms postoperatively. In patients with symptomatic cholelithiasis, pathology demonstrated biliary calculi in all patients and a total of 303 (93%) of these patients experienced symptomatic resolution.

DISCUSSION

This study evaluated 432 patients who underwent cholecystectomy providing valuable insights into the pathological findings and outcomes associated with the subset of patients with biliary dyskinesia. Our results indicate a clear demographic and pathological distinction between patients diagnosed with biliary dyskinesia versus those with gallbladder calculus disease. The findings also underscore the high efficacy of laparoscopic cholecystectomy in treating biliary dyskinesia.

Patients diagnosed with biliary dyskinesia were significantly younger than those with gallbladder calculus disease (46 vs 55 years), and a higher proportion were women. This aligns with existing literature suggesting that biliary dyskinesia may be more prevalent in younger women, potentially reflecting hormonal or metabolic factors influencing gallbladder motility.[18] The lower BMI in the biliary dyskinesia cohort may suggest different underlying mechanisms or risk factors compared to those with gallbladder calculi, where a higher BMI is often observed.

The pathological examination revealed that most patients with biliary dyskinesia had chronic cholecystitis (83%), with a substantial proportion also exhibiting cholesterolosis (27%). These findings highlight that while biliary dyskinesia is a functional disorder, it often coexists with inflammatory and metabolic changes within the gallbladder.[19]

Table 2.
Preoperative Symptoms and Workup in Patients Undergoing Cholecystectomy for Biliary Dyskinesia

Variable	Biliary Dyskinesia n = 89	Male n = 7	Female n = 82	*P*
Symptoms				
Abdominal pain (%)	86 (96.6%)	7 (100%)	79 (96.3%)	.68[a]
Nausea/Vomiting (%)	34 (38.2%)	3 (42.9%)	31 (37.8%)	.81[a]

[a]Mann-Whitney *U* test, percentages in (%) represent columnar group percentages.

Table 3.
HIDA-CCK Results for Diagnosis of Biliary Dyskinesia

Variable	Biliary Dyskinesia n = 89	Men n = 7	Women n = 82	*P*
% EF, median [IQR]	18 [11–27]	27 [15–35]	17 [11–27]	.25[a]
Hypo- versus Hyperkinetic				.22[b]
EF <40% (%)	86 (97%)	6 (86%)	80 (98%)	
EF >80% (%)	3 (3%)	1 (14%)	2 (2%)	

[a]Mann-Whitney *U* test, percentages in (%) represent columnar group percentages.
[b]Fisher's exact test.

Table 4.
Intraoperative and Postoperative Outcomes in Patients with Biliary Dyskinesia

Variable	Biliary Dyskinesia n = 89	Men n = 7	Women n = 82	*P*
Intraoperative gallstones present (%)	9 (10%)*	1 (14%)	8 (10%)	.70[a]
Pathology				
Normal (%)	9 (10%)	0 (0%)	9 (11%)	.35[a]
Chronic cholecystitis (%)	75 (84%)	7 (100%)	68 (83%)	.29[a]
Cholesterolosis (%)	24 (27%)	2 (29%)	22 (27%)	.97[a]
Cholelithiasis (%)	11 (12%)*	2 (29%)	9 (11%)	.20[a]

[a]Mann-Whitney *U* test, percentages in (%) represent columnar group percentages.
*Five specimens indicated gallstones which were not found at pathology, bringing the total incidence of gallstones to 18%.

The diagnostic criteria used in this study, including HIDA scan results and clinical symptoms, effectively identified patients with biliary dyskinesia. A majority of the patients presented with hypokinetic biliary dyskinesia, consistent with prior studies. However, the identification of hyperkinetic dyskinesia in a small subset suggests that the functional impairment in these cases might differ significantly. The overall symptom resolution rate of 100% following cholecystectomy in this cohort is notable and supports the efficacy of the surgical intervention for this condition. Though, this may be due to short follow-up and in another study we found 85% resolution of symptoms long-term for patients with biliary dyskinesia.[20] Of note, our prior study had a low number of patients compared to the current and the follow-up postop questionnaire is limited as the cause of the recurrence of the abdominal pain is not delineated. For example, after our prior publication, we were able to do a virtual visit with one of the patients who clearly had costochondritis and resolution of the initial symptoms, but on the questionnaire had noted no resolution of the abdominal pain due to the new symptoms due to costochondritis.

Despite the successful outcomes, our current study highlights the ongoing challenges with the diagnostic process. The high resolution rate observed postoperatively may be partially attributed to the comprehensive preoperative workup, including EGD to rule out gastric pathology who do not have isolated right upper quadrant abdominal pain as many patients have epigastric pain alone. The resolution rate of 93% in the symptomatic cholelithiasis cohort suggests that in similar pathology, a greater sample size maintains that cholecystectomy is highly effective in resolving symptomatic biliary disease. Additionally, given 18% of patients had gallstones found intraoperatively or postoperatively with pathology indicates false negatives with ultrasounds are not uncommon with literature suggesting as much as 7%–7%.[21–23] Nonsurgical interventions are unexplored, with random-clinical trials indicating most patients will opt for surgery due to a dearth of alternative treatments.[24]

Our pathologic findings along with symptom resolution reinforce the effectiveness of laparoscopic cholecystectomy for treating biliary dyskinesia, but also underscores the need for a more nuanced diagnostic approach to

mitigate the challenges aforementioned. While this study offers valuable insights, there are limitations that warrant consideration. The retrospective design and reliance on preoperative diagnostic criteria might introduce biases in patient selection and diagnosis, as well as lead to data quality problems such as consistency and completeness. This study has a relatively small sample size when compared to incidence of gallbladder calculus disease globally, which is estimated to inflict 6% of the world's population, and incidence of cholecystectomies within the United States.[25,26] This limits our statistical power and could be contributing to the higher rate of symptomatic relief observed. Furthermore, demographic analysis outside of sex and BMI was not performed, potentially overlooking the impact of ethnicity, socioeconomic status, and race on intervention. The inclusion criterion, and HIDA protocol differs significantly from other studies which contributes to the great variation observed between independent single-institution studies on biliary dyskinesia.[27] Additionally, the lack of long-term follow-up data prevents assessment of the durability of symptom resolution and potential recurrence of symptoms, limiting time-to-recurrence analysis.

CONCLUSION

This study confirms that laparoscopic cholecystectomy is highly effective in resolving symptoms of biliary dyskinesia. Structural abnormalities were seen for the vast majority of patients with biliary dyskinesia, indicating that this is not just a functional issue, but also confirms that structural abnormalities are a manifestation of what is considered a functional disease. However, the overlap with structural gallbladder pathology and the challenges associated with current diagnostic methods highlight the need for ongoing evaluation and improvement in the diagnostic and treatment approaches for this condition. Efforts should be made to enhance diagnostic accuracy to minimize unnecessary surgical interventions.

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