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Biliary Dyskinesia and Symptomatic Gallstone Disease in Children: Two Sides of the Same Coin?

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Abstract

Background—Despite lack of consensus criteria, biliary dyskinesia (BD) is an increasingly accepted pediatric diagnosis.

Aims—We compared patient characteristics, outcomes, and resource utilization (before and after surgery) between children with BD and symptomatic cholecystolithiasis (LITH).

Methods—Data from the electronic medical record were abstracted for children diagnosed with BD or LITH between December 1, 2002, and November 30, 2012, at Children's Hospital of Pittsburgh.

Results—Four hundred and ten patients were identified (BD: 213 patients, LITH: 197 patients). Patients with BD had significantly lower BMI, longer symptom duration, more dyspeptic symptoms, and were more likely to present with other symptoms. Forty-one patients (13.8 %) with BD underwent cholecystectomy despite a normal gallbladder ejection fraction (GB-EF). In 32 of these, sincalide triggered pain compared to 75 of the 155 patients with low GB-EF. After surgery, patients with BD more commonly visited gastroenterology clinics and had more GI-related hospitalizations, while emergency room visits decreased in both groups. Only the nature of biliary disease independently predicted continuing pain after surgery, which in turn was the best predictor for higher resource utilization after cholecystectomy.

Conclusions—A large percentage of children with BD did not meet the adult diagnostic standards. Compared to those with LITH, children with BD have more widespread symptoms and continue to use more clinical resources after surgery. These findings suggest that despite its benign

prognosis, BD is increasingly treated like other potentially acute gallbladder diseases, although it has the typical phenotype of FGIDs and should be treated using approaches used in such disorders.

Keywords

Biliary dyskinesia; Cholecystolithiasis; Cholecystectomy; Functional gastrointestinal disorders

Introduction

Functional gastrointestinal disorders (FGIDs) account for over half of pediatric gastroenterology consultations in the US [1]. Most of the recognized disorders are defined based on a characteristic symptom constellation and its impact of quality of life. While changes in transit, sensory function, or contractile patterns have been described as mechanisms or biomarkers of FGIDs, the correlation between results of physiological testing and symptoms is frequently limited. Thus, the most recently revised classification of FGIDs shifted away from mechanistic to a descriptive terminology [2, 3]. Biliary dyskinesia (BD) is an exception from this trend as it attributes intermittent right upper abdominal pain to abnormalities in gallbladder function, established by a documented impairment of gallbladder contraction in response to pharmacological stimulation [4]. Pain with a specific character and location is thus one of the defining criteria in BD. About 10 % of children with functional abdominal pain will locate the discomfort to the right upper abdomen, raising concerns about a potential biliary cause [5]. Gallstone disease remains uncommon in children [6]. The introduction of functional gallbladder testing and acceptance of BD in adults led to an apparent shift in pediatric practice. Even though BD has not been included in the list of pediatric FGIDs catalogued by the Rome III consensus group [7], the diagnosis is made increasingly often and BD now accounts for up to half of the cholecystectomies in pediatric centers [8–12]. Yet, only one study has evaluated this approach in a randomized controlled trial that enrolled adults only [13]. While the results favored cholecystectomy, the control group did not receive any active therapy and did not show any improvement, a highly unusual finding in functional disorders [13]. The results also differ from reported outcomes in BD, which are more variable with decreasing success rates after longer follow-up time and which include response rates exceeding 50 % in patients who did not undergo surgery [12, 14–28].

Longitudinal studies demonstrated that FGIDs have a benign course [29]. However, the often significant negative impact on quality of life [30–34] and the resulting healthcare seeking behavior [35–37] may lead to many interventions including surgery [38]. Based on these findings, we hypothesized that BD as a functional gastrointestinal disorder is associated with other syndromes characterized by pain and high healthcare resource utilization prior to and after cholecystectomy. Using a large cohort of children operated for BD or symptomatic cholecystolithiasis (LITH) as disease controls, the objectives of this study were to retrospectively (1) characterize patients with BD in comparison to those with LITH, (2) compare symptom response to cholecystectomy between patients with BD and LITH, and (3) compare healthcare utilization between patients with BD and LITH.

Materials and Methods

The study was designed as a retrospective review of inpatient and outpatient encounters at Children's Hospital of Pittsburgh. Because BD does not have its unique ICD 9 code, patients were identified based on the International Classification of Diseases (ICD) 9 code 575.80 (gallbladder disease not elsewhere specified), which accounts for most of the adult and pediatric patients with BD [39]. Pediatric patients with LITH were chosen as the control group and identified based on the ICD 9 codes 574.20 (cholecystolithiasis without obstruction). The study period covered 10 years (12/1/2002–11/30/2012). The protocol was reviewed and approved by the Institutional Review Board of the University of Pittsburgh (PR13010189).

Inclusion Criteria

All individuals included in the study had to be between 2 and 21 years at the time of the index encounter. For patients with BD, the diagnosis was based on the documented presence of abdominal discomfort thought to be biliary in origin in the absence of stones or sludge in the gallbladder as assessed by ultrasound. Patients with LITH similarly had to experience discomfort but had documented stones in the gallbladder.

Exclusion Criteria

Patients with developmental delay or disability, or significant organic comorbid conditions that could manifest with abdominal pain (e.g., pancreatitis, inflammatory bowel disease, nephrolithiasis) were excluded. In the group with symptomatic gallstone disease, we focused on cholecystolithiasis only and did not include patients with choledocholithiasis or underlying acute inflammatory or hereditary diseases of the biliary tree.

Data Abstraction

Using the electronic medical record, we abstracted demographic information [age at the time of diagnosis, sex, relative body mass index (BMI) as Z score], co-existing medical conditions, symptoms, symptom duration, diagnostic tests with results, and for patients in the BD group, the results of functional gallbladder testing. In order to capture resource utilization prior to and after cholecystectomy, we examined the number of encounters in relevant specialty clinics (gastroenterology and surgery), emergency room (ER) encounters, and hospitalizations for the 12 months prior to and after cholecystectomy. For encounters after the incident cholecystectomy, the documented presence or absence of abdominal pain or other gastrointestinal symptoms was noted. These encounters were grouped into four distinct time domains (1, 3, 6 and 12 months after surgery).

Data Analysis

Descriptive statistics were used to characterize both disease groups and their symptomatic outcomes after surgery. Disease group comparisons were made using chi-square and *t* tests for dichotomous and continuous variables, respectively. In order to identify potential predictors of abdominal pain after cholecystectomy for BD, we performed a logistic regression analysis, entering symptom duration, the presence of a low GB-EF, symptoms with sincalide, comorbid chronic headaches or affective spectrum disorders, and prior ER

visits. To identify potential predictors of abdominal pain after cholecystectomy in the entire cohort (both disease groups), we performed a logistic regression analysis, entering diagnosis, gender, the presence of symptoms for greater than 3 months, dyspeptic symptoms, prior ER visits, headaches, and hemolytic anemia.

For the healthcare utilization analysis, as utilization parameters were not normally distributed, the Wilcoxon Signed-Rank test was utilized to compare utilization parameters within disease groups 1 year before compared to 1 year after cholecystectomy. We performed univariate analyses, relating healthcare resource utilization with demographic and clinical data. Variables with a $P < 0.1$ were entered into a logistic regression analysis to identify independent predictors of the presence of ongoing resource utilization. Considering the disease-defining criteria of symptom duration and low GB-EF, we dichotomized results (symptom cutoff: 3 months; GB-EF cutoff: 40 % based on the consensus criteria defined for adults [4]) and assessed their utility as potential predictors. In addition, we examined the potential prognostic value of symptoms during pharmacological stimulation with the cholecystokinin (CCK) analog sincalide, which has been proposed as a more important marker of biliary problems in adults with presumed BD [40, 41]. Unless indicated otherwise, all data are given as mean $\pm$ standard errors.

All statistical analyses were performed using SPSS 21.0 (SPSS Inc, USA).

Results

Baseline Data

A total of 410 patients were identified based on our inclusion criteria. The group was nearly equally divided between the diagnoses with BD in 213 and 197 with LITH. As shown in Table 1, patients with BD were more likely to be girls, had a slightly lower normalized BMI and had longer symptom duration. Liver enzymes were assessed in 172 (80.8 %) children with BD. Results were normal in all but two cases, which were attributed to a viral syndrome ($n = 1$) and biopsy-proven non-alcoholic fatty liver disease ($n = 1$). All but six patients with BD (six girls; age: 12.8 ± 1.4 years) underwent cholecystectomy. Considering the young age of the cohort, relatively few patients had significant comorbid conditions. Nonetheless, there were differences between the groups with BD patients having more problems with chronic headaches, while children with LITH were more likely to suffer from hemolytic anemia (Table 1). Pain was the primary clinical manifestation in all patients. In patients with BD, the pain was significantly more likely located in the right upper quadrant (132; 61.9 %) than in patients with LITH (83; 42.1 %; $P < 0.01$). An epigastric location ($n = 29$) or postprandial symptom exacerbation led to the clinical suspicion of biliary cause in the remaining BD patients. BD was associated with a higher number of other gastrointestinal complaints (Table 1).

As consensus criteria for the diagnosis of BD in adults include symptom duration of at least 3 months [4], we examined the fraction of children meeting this criterion. Nearly one-third of the cohort (70; 30.6 %) had symptoms for a shorter period of time. Considering the defining role of gallbladder functioning in BD, 82.1 % of the cohort had a gallbladder ejection fraction (GB-EF) of less than 40 %. The remaining 41 patients underwent

cholecystectomy despite a normal GB-EF. In 31 of these, the CCK analog had triggered pain compared to 89 of the 188 patients with low GB-EF ($P < 0.01$). Combining GB-EF and symptom duration, a total of 94 (44.1 %) patients underwent cholecystectomy, even though their presentation was not consistent with the currently accepted diagnostic criteria of BD for adults.

The microscopic examination of the removed gallbladder in the patients with BD demonstrated normal findings in 80.8 %. Mostly mild inflammation was described in 14.9 %, cholesterosis in 1.9 % with the remainder having gallbladder thickening or incidentally identified duplication of the gallbladder. In contrast, 47.9 % of the patients with LITH had cholecystitis based on microscopic assessment ($P < 0.01$).

Symptomatic Outcome

Within the first month after surgery, 183 BD (85.9 %) and 142 LITH (72.1 %) patients were seen in clinics or the ER, enabling us to assess postoperative changes in symptoms as reported in the medical record. An additional seven BD and eight LITH patients were not reevaluated within month after surgery, but had clinic encounters at later time points. Two of the six conservatively treated children had follow-up encounters—one had partial relief of presenting abdominal pain with amitriptyline, proton pump inhibitor, and antispasmodic treatment at 3-month follow-up, and the other patient was noted to have pain resolution at 6-month follow-up with proton pump inhibitor and antispasmodic therapy. There is no record of follow-up for the remaining four of the six conservatively treated patients after the diagnosis of BD was made. Out of the operated cohort, 129 BD (70.5 %) and 124 LITH (87.3 %) children reported symptom resolution at 1 month ($P < 0.01$). In the BD cohort, half of the individuals with continuing symptoms were seen at a later time point with only one reporting being pain free. Conversely, 28 of the children with initial symptom resolution had additional ER visits or clinic encounters; at 3 months, 10 of 14 complained about recurrent pain, at 6 months 14 of 16 had ongoing problems, and 12 months, nine of 12 were symptomatic. In contrast, only seven LITH patients with residual pain at the first month had subsequent clinic encounters with three continuing to experience discomfort. Follow-up of patients with initial improvement was limited with only nine individuals being seen at later time points; at 3 months, three of nine had pain, at 6 months, four of five, and at 12 months, three of three had continuing abdominal pain. Focusing on the documented presence of ongoing abdominal discomfort at the last clinic encounter within the 12-month period after surgery, a total of 80 BD (42.1 %) compared with 26 LITH (17.3 %) patients had at least some ongoing abdominal discomfort ($P < 0.01$).

In order to identify potential predictors of poor outcome after cholecystectomy for BD, we performed a logistic regression analysis, entering symptom duration, the presence of a low GB-EF, symptoms with sincalide, comorbid chronic headaches or affective spectrum disorders, and prior ER visits. None of these variables significantly correlated with persisting pain after surgery (Table 2). When examining the entire cohort, only the diagnosis of BD independently predicted continuing pain after cholecystectomy (Table 3).

Resource Utilization

Patients with BD underwent significantly more diagnostic tests and were more likely to undergo medical treatment prior to surgery (Table 1). Medical therapy had been tried in 58.5 % of the cohort and mostly relied on proton pump inhibitors. Nearly one-third of the group (29.6 %) had received more than one drug therapy prior to surgery. In contrast, only 26 (13.2 %) of the children with LITH were taking proton pump inhibitors.

Prior to the index cholecystectomy, 97 (49.2 %) of LITH patients had at least one ER visit compared with 66 (31.0 %) of children with BD ($P < 0.01$). After cholecystectomy, ER visits decreased significantly and did not differ between the groups (Fig. 1). Hospitalizations were similar for both cohorts before surgery and significantly decreased in LITH ($P < 0.05$) but not in BD after surgery (Fig. 1). Significantly more children with BD had clinic encounters with gastroenterologists and surgeons prior to cholecystectomy and continued to see gastroenterologists more often than LITH patients after surgery (Fig. 1). As the initial visit in surgery clinics is often a routine check and thus a poor surrogate for ongoing healthcare needs, we assessed the total number of patients who had at least one additional encounter in the ER, hospital, or clinical setting. Children with BD ($n = 82$; 38.5 %) were significantly more likely than LITH patients ($n = 43$; 21.8 %; $P < 0.01$) to continue using healthcare resources.

We next performed a logistic regression to identify factors contributing to ongoing healthcare resource utilization. Focusing on children with BD only first, documented abdominal pain after surgery was the best predictor of continuing need for ER visits or clinic encounters after cholecystectomy (odds ratio 7.76; 95 % confidence interval 3.58–16.84). As was true for postoperative pain persistence, none of the disease-defining or proposed prognostic variables correlated with ongoing need for medical services. Similarly, ongoing pain also predicted continuing medical needs for the entire cohort (Table 4).

Discussion

Our study confirms that BD has become a common indication for cholecystectomy in children. While we did not determine the total number of cholecystectomies performed during the study period, the cohort of patients with this functional disorder was larger than that with symptomatic gallstone disease and increased from 23.0 ± 3.8 % of the entire cohort during the first 5 years to 59.6 ± 4.5 % during the last 5 years. The results thus fit into the emerging pattern with an increasing number of pediatric cholecystectomies being performed for BD nationwide [20, 28, 42–44]. Despite the apparent acceptance of BD as indication for surgery, outcomes are not as good as those in patients with gallstones; about 40 % of the children continued experiencing abdominal discomfort, and healthcare resource utilization remained high. Persisting pain was the only independent predictor for ongoing healthcare needs; pain in turn was best predicted by the BD as the underlying diagnosis. Equally important is what did not predict persistent pain or higher healthcare resource utilization, as the presumably disease-defining abnormalities, a low GB-EF, or the symptomatic response to the CCK agonist, were not useful prognostic indicators [28, 40].

While limited by the retrospective design, our approach is unique, because we included a disease control, cholecystolithiasis, which is obviously distinct with its defining structural abnormalities, but has similar symptoms, and at least in our cohort was also treated identically. This strategy enabled us to compare outcomes, resource utilization, and also potentially important phenotypic differences between two groups with similar age distribution, a clear female predominance, and pain as the primary symptom. The most striking difference is the longer duration of symptoms, which likely contributes to the more common use of medical therapies in BD. This apparent delay may suggest that surgery functioned as a last resort when conservative therapies failed. We can obviously not definitively address this point. The relatively high number of children receiving only one type of or even no medical treatment argues against this interpretation as being valid for a significant number of cases. In addition, only six patients were treated conservatively, which is a smaller number than previously reported in other studies and suggests a relatively low threshold for surgical referral and intervention [12, 19, 21, 45].

More children with BD had additional gastrointestinal complaints and also suffered more frequently from chronic headaches, which certainly fits the pattern of functional disorders [46]. However, we did not find an increase in clinically manifest mood disorders, which are not only commonly associated with FGIDs, but may indeed be an important mechanism for the development of these diseases [47]. While the use of antidepressants was higher in BD, the majority received tricyclic antidepressants targeting the abdominal pain rather than a possibly underlying affective spectrum disorder. Considering the retrospective design of our study, we cannot exclude differences in anxiety and depression, as systematic assessments were not performed.

Our findings demonstrate a less convincing benefit of surgery compared to many previously published case series which generally endorsed the use of cholecystectomy for BD with most authors reporting improvement in 70–100 % [42, 48–51]. However, response rates decrease over time and are quite similar to our results [14, 28, 45, 52–54]. Importantly, recent evidence suggests that despite high rates of symptomatic improvement soon after surgery, conservative therapy may be equally effective if not superior to cholecystectomy, when children were followed over longer periods of time [12, 14]. Others have demonstrated that the two most commonly used diagnostic criteria, a low GB-EF or pain triggered by sincalide infusion, did not predict postoperative outcomes [45, 48, 52], which is certainly consistent with our findings based on the largest cohort examined as of yet. These negative results led to suggestions to choose an even lower cutoff as defining criteria for BD [14, 28]. While the results of uni- and multivariate analyses argue clearly against the utility of gallbladder function as prognostic marker, one could question whether different results may be obtained using such presumably more stringent criteria. Lowering the cutoff to a GBEF of less than 15 %, about one quarter of our sample ($n = 56$) fell into this category. Due to concerns about the low power of this relatively small subgroup, we did not perform separate multivariate analyses. However, pain persistence recorded during the last clinic encounter was at 39.3 % ($n = 22$) and thus comparable with the data for the entire group. Such post hoc analyses by definition do not include healthy volunteers or—even more importantly—disease controls. In the absence of a true “gold standard,” data on the performance

characteristics in such reference populations are needed to decide on cutoffs with acceptable sensitivity and specificity. Some of these data have been obtained in adults and are the basis for the currently used definition of normal values. Yet, a detailed assessment by Delgado-Aros et al. [55] concluded that functional gallbladder testing does not meet criteria for a clinically useful prognostic test, as we now also show for pediatric patients.

BD has not been included in the most recent consensus document defining FGIDs in children [56]. Thus, we can only assess whether patients included in our study met disease-defining criteria described for adults [16]. The key points include intermittent episodes of pain with a character, location, and radiation suggesting a possible biliary etiology, some degree of chronicity, and the low GB-EF. While all patients included did complain about pain, the description did not provide sufficient details in all cases to appropriately address pain character, radiation, and/or its intermittent nature. Focusing on symptom duration and impaired gallbladder function, about 40 % of our cohort presented with a constellation that did not meet consensus criteria applied in patients. In some instances, the treating physicians relied on the fact that the cholecystokin analog triggered symptoms. As already mentioned above, this criterion has never been systematically evaluated. Nonetheless, several clinical investigators have proposed it as an appropriate selection criterion, proposing an even inherently contradictory terminology, such as “biliary dyskinesia without dyskinesia” [41]. Our findings in pediatric patients are consistent with recently reported data from adults [26, 57] and reflect the lowered threshold to proceed to cholecystectomy after introduction of minimally invasive surgery [58–60]. In addition, surgeons likely extrapolate from their experience with symptomatic or even complicated gallstone disease, which can and often does present acutely and may lead to complications, as also indirectly supported by the higher frequency of ER visits in LITH patients prior to surgery. Even though development of complications has never been shown for BD and is highly unlikely for a functional illness, but probably still affects clinical decision making through reasoning by analogy.

The higher rate of diagnostic testing in patients with BD compared to LITH suggests that the treating clinicians entertained alternative explanations, triggering for example endoscopic assessments in nearly 50 % of the cohort. A more consistent approach that systematically excludes other possible explanation of dyspeptic symptoms or upper abdominal pain, for example with endoscopy in all persons, would likely not have altered the approach, as truly relevant structural changes, such as peptic ulcer disease, are quite rare in the pediatric population [61].

We did not focus on the cohort of children operated for symptomatic gallstone disease but rather used it as disease control. Nonetheless, our results are consistent with other reports, showing a clear female predominance, a contribution of obesity, and a low fraction of children with pigment stones due to hemolytic anemia [62].

Our study describes the largest cohort of pediatric patients operated for BD and includes a disease control group, thereby providing different lines of support for our conclusions. Nonetheless, data acquisition was retrospective and thus by definition limited. We could not systematically assess the presence of ongoing abdominal complaints, but instead relied on the description of persisting pain documented during clinical encounters after surgery. As

many of these encounters took place in surgery clinics and involved the operating physician, we may overestimate the benefits of cholecystectomy due to a reporting bias. In addition, we did not capture interactions between patients and their pediatricians, but instead only analyzed clinical encounters that took place in the specialized care environment of a children's hospital and its affiliated clinics. Again, the result could be a low estimate of patients with recurrent or persistent symptoms. Despite these obvious caveats, the correspondence between symptom persistence or recurrence and continuing use of clinical services indirectly supports the validity of our findings. Lastly, the lack of any association between mood disorders and a FGID, in this case BD, has previously been reported in a smaller study [12] and is unusual, as such disorders commonly coexist in pediatric patients with functional illnesses [63]. We see these negative results as a consequence of our retrospective design, which relies on listed and clinically manifest mood disorders rather than the systematic assessment of anxiety and/or depression.

In conclusion, this large cohort study shows that children with BD have more widespread symptoms and thus fit a pattern of functional disease with likely overlap between various syndromes and ongoing impairment of quality of life [46, 64–68], driving continuing resource utilization. Considering the lack of known complications due to BD and the often spontaneous improvement with conservative therapies, these findings highlight the need to move away from surgical approaches and instead explore and apply treatment strategies used in other functional disorders.

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Fig. 1. Resource utilization in children with biliary dyskinesia (*black bars*) and symptomatic cholecystolithiasis (*gray bars*) before and after cholecystectomy. Significance was assessed using group comparison with chi-square statistics. *GI Clinic* gastroenterology clinic. *Surg Clinic* surgery clinic

Table 1

Baseline characteristics of patients with BD and LITH

	Biliary dyskinesia (<i>n</i> = 213)^a	Cholecystolithiasis (<i>n</i> = 197)	<i>P</i>
Age	14.72 ± 0.17	13.89 ± 0.26	0.09
Sex (% females)	172 (80.8 %)	70.6 %	0.02
BMI (Z score)	0.90 ± 0.08	1.16 ± 0.09	0.01
% Overweight (BMI Z score ≥ 1)	105 (49.2 %)	55.33 %	0.02
% Obese (BMI Z score ≥ 1.65)	64 (30.0 %)	37.1 %	0.04
GB-EF (%)	28.88 ± 1.70	n/a	
< 40 %	155 (72.80 %)		
Pain response with CCK analog	113 (53.10 %)		
Presenting symptoms			
Abdominal pain	100 %	100 %	1.00
Abdominal pain duration (mo)	7.88 ± 0.99	3.52 ± 0.56	< 0.001
Abdominal pain < 3 mo	67 (31.4 %)	92 (46.7 %)	< 0.001
Nausea/vomiting	55 (25.8 %)	65 (33.0 %)	0.10
Bloating	13 (6.1 %)	1 (0.5 %)	0.002
Constipation	9 (4.2 %)	1 (0.5 %)	0.02
Diarrhea	18 (8.5 %)	5 (2.5 %)	0.01
Weight loss	24 (11.3 %)	7 (3.6 %)	0.003
Comorbidities			
GERD	23 (10.8 %)	11 (5.6 %)	0.07
Depression	12 (5.6 %)	8 (4.1 %)	0.42
Anxiety	12 (5.6 %)	7 (3.6 %)	0.26
Headaches	37 (17.4 %)	9 (4.6 %)	< 0.001
Hemolytic anemia	0 (0.0 %)	29 (14.7 %)	< 0.001
Diagnostic testing			
Ultrasound	212 (99.5 %)	197 (100.0 %)	1.0
Endoscopy	103 (48.4 %)	6 (3.0 %)	< 0.001
Colonoscopy	36 (16.9 %)	0 (0.0 %)	< 0.001
UGI contrast study	26 (12.2 %)	1 (0.5 %)	< 0.001
Gastric emptying study	9 (4.2 %)	0 (0.0 %)	< 0.05
Therapy			
PPI	115 (54.2 %)	26 (13.2 %)	< 0.001
Spasmolytic	42 (19.7 %)	0 (0.0 %)	< 0.001
TCA	16 (7.5 %)	0 (0.0 %)	< 0.001
Cyproheptadine	14 (6.6 %)	0 (0.0 %)	< 0.001

^aIncludes six conservatively treated patients with BD (significance values refer to bivariate comparisons)

Table 2

Independent predictors of postoperative pain in children with biliary dyskinesia based on logistic regression analysis

Variable	Odds ratio	95 % confidence interval
Symptoms > 3 months	0.67	0.31–2.16
Dyspeptic symptoms	1.01	0.50–2.02
Prior ER visit(s)	1.03	0.49–2.15
Mood disorder	0.53	0.17–1.68
Headaches	0.89	0.36–2.21
GB-EF < 40 %	1.14	0.47–2.78
Pain response with CCK analog	1.37	0.60–3.15

Table 3

Independent predictors of postoperative pain based on logistic regression analysis

Variable	Odds ratio	95 % confidence interval
Biliary dyskinesia	2.73	1.42–5.22
Sex	1.13	0.57–2.23
Symptoms > 3 months	1.27	0.69–2.33
Dyspeptic symptoms	0.85	0.49–1.47
Prior ER visits	0.86	0.48–1.56
Headaches	0.98	0.44–2.18
Hemolytic anemia	0.01	0.001–10.0

Table 4

Independent predictors of postoperative resource utilization based on logistic

Variable	Regression analysis	
	Odds ratio	95 % confidence interval
Biliary dyskinesia	1.98	1.12–3.48
Sex	0.88	0.45–1.54
Symptoms > 3 months	1.23	0.71–2.13
Dyspeptic symptoms	1.09	0.66–1.81
Prior ER visits	1.64	0.95–2.83
Headaches	1.40	0.66–2.95
Hemolytic anemia	0.86	0.22–3.38