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## Outcomes in Children and Adolescents Undergoing Cholecystectomies with a High Ejection Fraction

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# ***Outcomes in children and adolescents undergoing cholecystectomies with a high ejection fraction.***

*Salony Dighamber BS, Karen Herzing, RN, Arturo Aranda, MD, Jeffrey Pence, MD, Sean Barnett, MD*

## **ABSTRACT**

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### ***Background***

Cholecystectomy is commonly performed electively for symptomatic cholelithiasis and biliary hypokinesia with an ejection fraction (EF) less than 35%. Recent literature has shown that cholecystectomy in adults for biliary hyperkinesia (EF>65%) can provide resolution of symptoms (primarily pain) for the majority of patients. We seek to determine whether cholecystectomy is efficacious in the treatment of symptomatic biliary hyperkinesia in the pediatric population.

### ***Method***

The charts of over 100 patients aged 7 to 21 in the last 10 years (2008 to 2018) who had cholecystectomies were reviewed to determine ejection fraction, BMI, race, pain with CCK-HIDA, complications, and resolution of symptoms (pain, vomiting, steatorrhea, diarrhea) post operatively. Analyses of surgical outcomes were performed between two groups, low/normal EF and high EF, which were stratified and compared.

### ***Results***

A total of 79 patients had low/normal EF (EF <65%), and 26 had high EF (EF>65%). Mann-Whitney, Chi-square, & Fisher's exact tests differentiated between groups. The resolution of symptoms rate was similar between groups with no statistical difference: low/normal EF (75%) vs. high EF (69%), p=0.497. Pain with HIDA scan appeared higher in the high EF group (p=0.047), refer to *Table 1*. No difference was shown between groups for gender, race, age, BMI, and follow-up rates. No surgical complications were seen in either group.

### ***Conclusion***

Pediatric patients with symptomatic biliary hyperkinesia experience a similar rate of resolution of their symptoms when compared to similarly matched patients who underwent cholecystectomy for biliary hypokinesia.

## **INTRODUCTION**

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Laparoscopic cholecystectomies have traditionally been used to remove gallbladders with ejection fractions less than 35 percent, or hypokinetic gallbladders. Recently, this surgery is being used for patients with biliary pain that is not due to a hypokinetic gallbladder. Hyperkinetic gallbladders are classified as gallbladders with ejection fractions greater than typically 80 percent.<sup>4</sup> While the majority of research has been done on hypokinetic gallbladders, more recent studies have shown that patients with hyperkinetic gallbladders are benefitting from receiving laparoscopic cholecystectomies.<sup>1,3,4,5</sup>

In a study of 23 patients with hyperkinetic gallbladders, results following surgery showed 88.2 percent improvement in biliary pain.<sup>5</sup> In addition, much like the other articles, a CCK HIDA provocation test was used to see if pain during the test was an indication for cholecystectomy, which it was.<sup>2,5</sup> In a case study with two adults, a 28-year-old woman with an ejection fraction of 95 percent and a 21-year-old woman with an ejection fraction of 90 percent, underwent cholecystectomy, and both patients had improvement of symptoms afterwards.<sup>1</sup>

The patient population used in both of the aforementioned studies were adults. In a case study of three adolescent patients, 16, 18, and 13, with ejection fractions of 81, 72, and 77, respectively, underwent surgery and also had complete resolution of symptoms.<sup>3</sup> Another study even showed that a pediatric patient population with ejection fractions of 80 percent or greater experienced relief of pain as discussed with their parents over the phone.<sup>4</sup> The population studied, while limited, had all shown chronic cholecystitis via final pathological examination.<sup>4</sup>

In a final article discussing "normokinetic" gallbladders, patients did not have a hyperkinetic gallbladder, they did have reproducible pain during a CCK-HIDA and with an ejection fraction greater than 35 percent.<sup>2</sup> It was found that this an indication for cholecystectomy, as there was an overall improvement of 94.7 percent among these patients.<sup>2</sup>

Laparoscopic cholecystectomies have been the mainstay of definitive treatment for symptomatic cholelithiasis and biliary dyskinesia for years. In the more recent years, however, the discussion of laparoscopic cholecystectomies for the use of hyperkinetic gallbladders has become a topic of debate as data on the subject is limited, especially in the pediatric population.

The passage of bile from the gallbladder and into the duodenum is regulated by the structure of the biliary ducts and hormones.<sup>2</sup> The anatomy of the gallbladder and the biliary tree requires an open lumen that allows for the flow of bile. If this is obstructed in any way, inflammation results and patients experience pain. Cholecystokinin (CCK) is a neurohormone released by the duodenal lumen in response to amino acids and fats, stimulating the gallbladder to contract. The degree of gallbladder volume change and intraluminal pressure in the gallbladder is directly proportional to the amount of CCK released by the duodenal lumen.<sup>2</sup>

Gallbladder motility decreases with age due to decreased sensitivity of the CCK receptors in the gallbladder.<sup>2</sup> With this knowledge we can make an assumption that in our pediatric patient population, sensitivity of the CCK receptors may be increased, leading to higher ejection fractions. Another potential cause of increased ejection fraction might be due to the increased release of CCK; however it is difficult to measure the amount of CCK released, again, due to difficulty in assessing in vivo CCK production.

The purpose of this study is to determine whether cholecystectomy is efficacious in the treatment of symptomatic biliary hyperkinesia in the pediatric population. Data on cholecystectomy outcomes on hyperkinetic gallbladders is scarce in this specific population; therefore, it is sensible to pursue research in this particular field.

## METHODS

The charts of 105 pediatric patients ages 7 to 21 from 2008 to 2018 who underwent cholecystectomy were retrospectively reviewed. A low ejection fraction was considered anything less than or equal to 35% and a high ejection fraction was considered anything that is greater than or equal to 65%. Anything in between was considered normal and will be grouped with the low ejection fraction group for comparison purposes.

Data was also collected on BMI, race, pain with CCK-HIDA, complications, and resolution of symptoms (pain, vomiting, steatorrhea, and diarrhea) postoperatively. Statistical analyses (Mann-Whitney, Chi-square, and Fisher's exact tests) were performed between two groups, low/normal EF and high EF, which were stratified and compared.

## RESULTS

A total of 79 patients had low/normal EF (EF <65%), and 26 had high EF (EF >65%). Mann-Whitney, Chi-square, & Fisher's exact tests differentiated between groups. The resolution of symptoms rate was similar between groups with no statistical difference: low/normal EF (75%) vs. high EF (69%),  $p=0.497$ . Pain with HIDA scan appeared higher in the low/normal EF group ( $p=0.047$ ), refer to *Table 1*. No difference was shown between groups for gender, race, age, BMI, and follow-up rates. Therefore, it can be assumed that these demographic factors did not make impact the outcome of the study. No surgical complications were seen in either group.

*Table 1:* Descriptive statistics for all patients and comparisons between patients with low/normal EF vs. high EF

Variable	Level	All patients No. (C%)	Patients with low/normal EF No. (R%) (C%)	Patients with high EF No. (R%) (C%)	P value
*Resolved symptoms	Yes	78 (74.3)	60 (76.9) (75.9)	18 (23.1) (69.2)	<b>0.497</b> <b>c</b>
	No	27 (25.7)	19 (70.4) (24.1)	8 (29.6) (30.8)	
	Total	105 (100)	79 (75.2) (100)	26 (24.8) (100)	
Follow-up (n/y)	No	34 (32.4)	29 (85.3) (36.7)	5 (14.7) (19.2)	0.099 <b>c</b>
	Yes	71 (67.6)	50 (70.4) (63.3)	21 (29.6) (80.8)	
	Total	105 (100)	79 (75.2) (100)	26 (24.8) (100)	
Pain with HIDA	No	17 (27.9)	16 (94.1) (34.8)	1 (5.9) (6.7)	<b>0.047</b> <b>f</b>
	Yes	44 (72.1)	30 (68.2) (65.2)	14 (31.8) (93.3)	
	Total	61 (100)	46 (75.4) (100)	15 (24.6) (100)	
*Days between HIDA and surgery	Median (IQR)	26 (35)	22 (30)	43 (58)	<b>0.003</b> <b>m</b>
	Mean (SD)	71 (177)	4 (99)	142 (290)	
	Range	1-1291	1-716	4-1291	
	n	91	66	25	

Statistically significant P values (P<0.05) are bolded for all analyses.

Categorical variables: R% = row percent; C% = column percent; c = chi-square test; f = Fisher's exact test.

\*Resolved symptoms includes resolution of pain, vomiting, steatorrhea, or diarrhea

\*\*continuous variable used Mann-Whitney test=m.

Table 2: Demographic statistics for all patients and comparisons between patients with low/normal EF vs. high EF

Variable	Level	All patients No. (C%)	Patients with low/normal EF No. (R%) (C%)	Patients with high EF No. (R%) (C%)	P value
<b>**BMI</b> (kg/m <sup>2</sup> )	Median (IQR)	27.8 (12.7)	28.3 (12.5)	27.1 (13.8)	0.774 m
	Mean (SD)	29.7 (9.9)	29.5 (8.8)	30.4 (13.4)	
	Range	13.6-73.7	15.4-55.4	13.6-73.7	
	n	83	65	18	
<b>**Age</b> (years)	Median (IQR)	14.0 (3.0)	14.0 (3.0)	15.0 (4.3)	0.593 m
	Mean (SD)	14.6 (2.7)	14.5 (2.8)	14.7 (2.5)	
	Range	7-21	7-21	9-18	
	n	105	79	26	
Race	White	88 (93.6)	67 (76.1) (91.8)	21 (23.9) (100)	0.677 f
	Black	5 (5.3)	5 (100) (6.8)	0 (0.0) (0.0)	
	Other	1 (1.1)	1 (100) (1.4)	0 (0.0) (0.0)	
	Total	94 (100)	73 (77.7) (100)	21 (22.3) (100)	

Statistically significant P values (P<0.05) are bolded for all analyses.

Categorical variables: R% = row percent; C% = column percent; c = chi-square test; f = Fisher's exact test.

\*Resolved symptoms includes resolution of pain, vomiting, steatorrhea, or diarrhea

\*\*continuous variable used Mann-Whitney test=m.

## DISCUSSION

The purpose of this study was to determine whether or not cholecystectomies would be efficacious in the treatment of hyperkinetic gallbladders. The lack of difference between the high EF and low/normal EF group shows that regardless of EF, the outcomes of the surgery appear to remain the same (i.e., both show similar patterns of symptom resolution). This indicates that ejection fraction may be an arbitrary limit for whether or not a patient receives a cholecystectomy. In addition, our study suggests that pain with CCK HIDA may be a better indication to perform a cholecystectomy in patients with biliary colic. Given that resolution rates were similar between the two groups, yet the high EF group experienced more pain with the HIDA scan, it is suggested that

In our population, pain with HIDA was higher in patients with high EF rather than low EF patients. In Huckaby, et al, chronic inflammation was visible on histopathologic observation of the hyperkinetic gallbladder specimens. Although we did not analyze the surgical specimens of our own patients, chronic inflammation may be what is causing pain in our population. With the aforementioned potential causes of the hyperkinetic gallbladder state, the chronic increased release of CCK and/or sensitivity of CCK receptors may lead to increased intraluminal pressure in the gallbladder itself, which can cause chronic inflammation.

Another significant result of our study was that the days between HIDA scan and surgery was higher in that of our hyperkinetic gallbladder population. A possible explanation this would be that in general, high ejection fractions are not seen as an immediate reason for cholecystectomies. On another note, having hyperkinetic gallbladder as an indication for cholecystectomies may lessen the grief and pain patients go through because it may decrease the time between HIDA scan and surgery.

Strengths of our study include the use of patients with gallbladders with normal/low EF as a control group. This is also the largest study evaluating cholecystectomies in hyperkinetic gallbladders in the pediatric population that we are currently aware of.

Possible limitations of this study are the retrospective study design and relatively small sample size. In addition, not every patient in our study had a CCK HIDA, and pathology reports were not reviewed. In the future, a larger sample size of pediatric patients undergoing cholecystectomies who have had HIDA scans and their pathology reports may be reviewed. Possible future directions include repeating this study with a larger population of individuals and perhaps across different hospitals. It is possible that the results are significant in the Dayton Children's population, but not other hospital systems.

## CONCLUSION

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Pediatric patients with symptomatic biliary hyperkinesia experience a similar rate of resolution of their symptoms when compared to similarly matched patients who underwent cholecystectomy for biliary hypokinesia.

No surgical complications were encountered in either cohort supporting cholecystectomy as a safe treatment option in symptomatic hyperkinetic gallbladder treatment.

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