



## Surgical outcome in patients with biliary colic and atypical workup findings



R.C. Wright<sup>\*</sup>, N. Thach, H. Pepper, R. Robles, R.J. Wright

Meridian Surgery Center, Puyallup, WA, USA

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### ABSTRACT

**Background:** Surgical response of patients with symptomatic biliary colic but atypical findings of gallbladder polyps, hyper-dynamic gallbladder and otherwise negative biliary workup are underrepresented in the literature from community practice.

**Methods:** A clinical outcome study with a retrospective design compared the short term and long term symptomatic improvement reported by patients with pre-operatively diagnosed biliary dyskinesia to all other biliary colic patients with atypical pre-operative diagnoses. All patients underwent surgery at Meridian Surgery Center from the years 2010–2017. 600 patients were reviewed for biliary dyskinesia, gallbladder polyps, hyper-dynamic gallbladder and negative workup.

**Results:** Short term and long term results were compiled from a total 182 patients. Short term response rates were assessed from 74 biliary dyskinesia, 40 hyperdynamic, 23 gallbladder polyps, and 45 negative workup patients. Long term responses were received from 19 biliary dyskinesia patients, 11 hyperdynamic patients, 9 polyp patients, and 7 negative workup patients.

Long term improvement among biliary dyskinesia patients was 84%, and 83% among patients with atypical findings, representing a long term drop in symptoms. There is no significant difference between symptom recovery of patients with biliary dyskinesia and those with another atypical diagnosis: hyperdynamic (82%), polyps (89%), negative workup (57%).

**Conclusion:** These results allow us to conclude that there is a comparable biliary colic improvement between biliary dyskinesia, gallbladder polyps, hyper-dynamic gallbladder and negative workup patients after cholecystectomy in both short term and long term follow up.

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### Introduction

Patients presenting with right upper quadrant pain and varying levels of nausea, bloating and pain after eating fatty foods are considered for biliary colic.<sup>3,8,10</sup> Often these patients experience biliary colic with gallstones or biliary dyskinesia and are considered for a cholecystectomy. A relatively high proportion of these patients experience pain relief. According to a study in 1998 on 218 patients with biliary dyskinesia, 94.5% experienced symptomatic relief after undergoing a cholecystectomy.<sup>3</sup> A study from 2018 indicated complete resolution of symptoms in 89.5% of patients with biliary dyskinesia who have shown traditional symptoms of cholecystitis and who have undergone a cholecystectomy.<sup>10</sup> Ultrasounds of the abdomen can diagnose stones or polyps.<sup>11</sup> A strong move toward

diagnosis using the ejection fraction of gallbladders has occurred in the last thirty years.<sup>2</sup> A HIDA Scan with cholecystokinin (CCK) measure the gallbladder output and report the gallbladder ejection fraction and is increasingly useful for diagnosing biliary disease, especially when ultrasound results are normal.<sup>5</sup> A HIDA scan with an ejection fraction less than 35% is considered hypo-dynamic gallbladder, also known as biliary dyskinesia—biliary colic without gallstones.<sup>1,3,6,8,10</sup> An ejection fraction of greater than 35% is considered normal. Pain with CCK administration has also been reported as more accurate than ejection fraction.<sup>10</sup>

Some patients, however, experience biliary colic despite having negative ultrasound and HIDA scan reports, making their journey to symptomatic relief less defined. The ultrasound may show polyps and that is considered to be a negative finding. Further workups are often ordered, including CT scans or endoscopies.<sup>11</sup> Patients with completely negative workups have recently been diagnosed with “normokinetic biliary dyskinesia”.<sup>6,10</sup> Investigation into the best manner to treat patients with normokinetic biliary dyskinesia has

<sup>\*</sup> Corresponding author.

E-mail address: [bob@meridiansurgerycenterwa.com](mailto:bob@meridiansurgerycenterwa.com) (R.C. Wright).

been an ongoing issue. One study published in 2012 found that 94.7% of these patients experienced symptomatic improvement after cholecystectomy.<sup>6</sup>

Pediatric surgeons have lead the way in describing a condition they term hyper-dynamic gallbladder, defined as an ejection fraction on a HIDA scan greater than or equal to 80%.<sup>9</sup> They have found a consistent resolution of biliary colic. The studies are small, although they are very encouraging and have lead many clinicians to proceed with cholecystectomy and reporting good results. These surgeons findings, however, are still a point of dispute and the recent guidelines from the nuclear diagnostic society are still labeling all HIDA scans with ejections fractions over 35% as normal.<sup>6,10</sup>

Gallbladder ultrasound may show “polyps” and confuse the clinician regarding the etiology of a patients’ colic, leading to inaction. Corwin, though, reports that of polyp patients who underwent cholecystectomy, 57% had stones, and only 31% actually had polyps.<sup>4</sup> For similar persons with polypoid lesions, guidelines by many European radiology societies now recommend symptomatic patients undergo cholecystectomy if no other alternative cause is found.<sup>11</sup>

Patients with biliary colic and a completely “negative workup” are frequently passed by for cholecystectomy. Many primary caregivers and gastrointestinal specialists treat these patients for a form of functional or irritable bowel syndrome and treat them with antispasmodics that have varying degrees of success.

It is common for a patient with biliary colic and a negative workup to have endured many tests, suffered months or years of discomfort and to receive multiple diagnostic opinions. In this study, retrospective review of clinical improvement in patients with biliary colic and atypical workup is compared to those who undergo cholecystectomy for diagnosed biliary dyskinesia.

## Materials and methods

Patients who have undergone a laparoscopic cholecystectomy at Meridian Surgery Center between 2010 and 2017 were considered for this study. Cases with a diagnosis of cholelithiasis were not considered and patients were organized by pre-operative test diagnoses. Ultrasound, HIDA scan, and CT scan results were reviewed for diagnoses. Patient diagnoses were either “biliary dyskinesia” or “atypical workup.” The atypical workup patients fell into other refined groups: hyper-dynamic gallbladder, gallbladder polyps (<6 mm in size), and biliary colic with normal studies. Biliary dyskinesia was defined as a HIDA scan of less than 35% ejection fraction. Hyperdynamic gallbladder was defined as a HIDA scan of greater than or equal to 80% ejection fraction.

Clinical charts were reviewed for postoperative pain response utilizing the last postoperative visit note, as well as the Transition of Care Summary to calculate improvement. Improvement is calculated as the sum of total resolution and partial improvement. Additionally, patients with longer than six month follow up were mailed a pre-operative and post-operative symptom questionnaire, including a visual analog pain scale to calculate long term improvement rate as well.<sup>7</sup> Patients who did not respond were then called and an approved 5 min phone script that coincided with the mailed questionnaires was used to fill out the questionnaire verbally. By IRB guidelines, limited attempts were made to contact patients. The rate of long term improvement was also calculated and compared against the short term improvement rate statistically. Demographics were collected, including age, sex, race, BMI, smoking status, and ASA class.

A data spreadsheet was generated and delivered to an independent statistician to analyze the short term and long term pain

improvements and to compare between diagnosis groups. The statistician also analyzed short term and long term differences in pain score pre-operatively and post-operatively between patients with biliary dyskinesia and patients with a negative workup, and defined subgroups. The Wilcoxon rank-sum test and Mann-Whitney *U* test were performed on the long term data.

The research proposal was presented to the Institutional Review Board (IRB) for review. After ensuring patient confidentiality in the research plan, the research was granted permission to proceed.

## Results

3.1.1. The study began with 600 patients who were filtered for the presence of research consent (425 patients). Patients who's ultrasound revealed gallbladder stones or adenomyosis were then removed, leaving 182 patients for study. These 182 patients were included for long term improvement rate calculation and then were sent questionnaires either via mail or phone call. The return rate for the questionnaires was 26%, 46 out of the 182 patients responded. Group one, biliary dyskinesia patients, and group two, atypical workup patients, had no significant difference between their improvement rates after undergoing cholecystectomy.

3.1.2. This study included 133 females and 49 males, with a mean age of 44.7 years (Table A.1a, A.1b). When compared to the polyps group, the biliary dyskinesia, hyper-dynamic, negative workup patients had significantly lower average ages (Table A.2b). Refer to Tables A.1 and A.2 for the demographics percentages.

### *Biliary dyskinesia*

Group one, patients with biliary dyskinesia, had a short term improvement rate of 84% ( $n = 74$ ) and a long term improvement rate of 84% ( $n = 19$ ). They had a mean decrease in pain score of 5.6 on a 10 point scale after surgery. Based on the pathology reports 94.6% had chronic cholecystitis, 5.4% had gallstones, 2.7% had polyps, 4.1% had normal findings. Comparison of short term and long term followup when compared with the polyps group showed a *p* value of 0.14 and 1.00, respectively.

### *Atypical workup*

Group two, 111 patients had atypical workups, had a and their improvement rate in the short term was 84% ( $n = 108$ ), whereas the overall long term improvement rate was 77% ( $n = 27$ ). In the long term findings, they had a mean drop of pain score of 5.7. Based on the pathology reports 98.2% had chronic cholecystitis, 6.3% had gallstones, 8.1% had polyps.

For the subgroups within the atypical workup group:

### *Hyper-dynamic gallbladder*

There were 40 hyper-dynamic gallbladder patients with a short term improvement rate of 90% ( $n = 40$ ), and a long term improvement rate of 82% ( $n = 11$ ). Based on the pathology reports, 100% had chronic cholecystitis, 5% had gallstones, 5% had polyps. The mean pain score decrease was 6.1. Comparison of short term and long term followup when compared with the polyps group showed a *p* value of 0.081 and 1.00, respectively.

### *Polyps*

23 patients were found to have gallbladder polyps pre-operatively and their short term improvement after surgery was 70% ( $n = 23$ ). The long term improvement was 89% ( $n = 9$ ). They

had a long term mean drop in pain score of 6.0. Based on the pathology reports 100% had chronic cholecystitis, 4.8% had gallstones, 26% had polyps.

#### Negative workup colic

45 patients had normal workup colic and of those patients the short term improvement rate was 87% (n = 45), the long term improvement rate was 57% (n = 7). Based on the pathology reports 95.8% had chronic cholecystitis, 8.3% had gallstones, 2.1% had polyps. The mean decrease in long term pain score was 5.0. Comparison of short term and long term followup when compared with the polyps group showed a p value of 0.11 and 0.26, respectively.

#### Discussion

Our study demonstrates that patients with biliary dyskinesia who underwent laparoscopic cholecystectomies had similar pain improvement as biliary colic patients with atypical workups, including polyps, hyper-dynamic gallbladder, and negative workups (Table A.3). Patients with biliary dyskinesia had a long term improvement rate of 84% after receiving surgery. Similarly, patients with hyper-dynamic gallbladder and other atypical workup subgroups showed a similar response rate. Many of these patients who responded to the study had a good response rate regardless of what preoperative testing showed (Table A.3).

A study done in 2018 by Pihl et al. demonstrated similar results.<sup>10</sup> Their study involved 1116 patients who underwent a laparoscopic cholecystectomy and compared those with hyperkinetic, normokinetic and hypokinetic gallbladder ejection fractions.<sup>10</sup> Within the biliary dyskinesia and hyper-dynamic patients (termed hyperkinetic in the Pihl study) patients, our study and the Pihl et al. case demonstrated similar long term success rates. The rate of symptomatic improvement between the biliary dyskinesia in our study and the Pihl study were 84% and 83% (p = 1.00), respectively. Similarly, the hyper-dynamic patients in our study showed an 82% improvement rate, while the Pihl et al. study demonstrated an improvement rate of 87% (p = 1.00). The negative workup patients, however, demonstrated fairly different success rates, with our data showing a 57% success rate, and the Pihl et al. study demonstrating a 78.9% success rate (p = 0.18).<sup>10</sup>

Our study also investigated the impact of laparoscopic cholecystectomies on patients whose tests revealed gallbladder polyps. Often polyps are considered a negative result in an ultrasound, leading to patients being passed over for surgery. The results shows, however, that 100% of the patients who had preoperative reports of polyps actually had chronic cholecystitis, which suggests that patients with symptomatic polyps could be considered for surgery. Only 26% of our patients' pathology reports stated polyps present in these patients. Similarly, in the Corwin et al. study, of the 42 patients who underwent a cholecystectomy, 57% had symptomatic cholelithiasis and 21% of the patients actually had the polyps that had been identified pre-operatively.<sup>4</sup> Notably, our post-operative pathology reports indicated a significantly lower rate of cholelithiasis in our polyps patients, with only 4.8% of patients having gallstones. Gallbladder polyps are not considered a high cancer risk, but according to the literature, they predict a relatively high gallstones risk which also indicates a risk of emergent deterioration. According to Corwin et al., symptomatic patients with polypoid lesions should be candidates for cholecystectomy so long as there are no other explanations for their symptoms and they are physically fit to undergo surgery.<sup>4</sup> He also suggested that polypoid lesions are indicative of other gallbladder dysfunction such as gallstones or inflammation.

Biliary colic patients with negative workups showed

comparable improvement to biliary dyskinesia patients after undergoing a cholecystectomy. These patients, despite having completely negative ultrasounds, HIDA scans and CT scans (if applicable), still had a 95.8% incidence of chronic cholecystitis in their pathology reports. Additionally, they had an 8.3% occurrence of cholelithiasis that had not been picked up in preoperative testing. Patients with a negative workup demonstrated a significantly higher proportion of GERD, or acid reflux, than the other patient groups. There is a substantial overlap between biliary colic and GERD symptoms, causing both patients and doctors to occasionally confuse the two. Therefore, patients with negative workups with pain that is indicative of gallbladder disease, without any other explanation for their symptoms, have experienced early symptomatic relief the same as biliary dyskinesia patients.

Similar to the Pihl et al. study, we both caused concern of reporter bias on patient pain scores due to the retrospective approach to our studies. Unlike that study, we were also limited by our poor questionnaire response rate in our long term improvement analysis, possibly due to the long length of the questionnaire. We were also limited by the IRB, whereas the Pihl et al. study was allowed to contact patients an unlimited number of times, we were only allowed to send one mailed questionnaire, make two phone calls, and send one email. Our short term and long term improvement rates were comparable except for the negative workup group.

#### Conclusion

In this single surgeon report of biliary colic patients with atypical workups including no gallstones and a negative HIDA scan, patients with polyps, hyper-dynamic gallbladder and negative workups responded as well to their laparoscopic cholecystectomy as patients with biliary dyskinesia.

#### Appendix A

Table A.1

Table 1a  
Patient demographics.

		N	%
Sex	Female	133	73%
	Male	49	27%
Race	Asian	4	2%
	Black	3	2%
	Hispanic	2	1%
	White	173	95%
Smoking status	Current	34	19%
	Former	56	31%
	Never	92	51%
ASA class	1	53	29%
	2	105	58%
	3	23	13%
	4	1	1%
GERD	No	117	64%
	Yes	65	36%

Table 1b  
Patient demographics.

	Mean	Standard Deviation
Age	44.7	14.6
BMI	29.5	6.5

Table A.2a. b

**Table 2a**  
Patient demographics by group.

	Group	Patient demographics by group										
		Biliary dyskinesia			Hyperdynamic gallbladder			Negative workup			Polyps	
		N	%	p-value* vs Polyps	N	%	p-value* vs Polyps	N	%	p-value* vs Polyps	N	%
Sex	female	59	80%	1.00	22	55%	0.10	34	76%	1.00	18	78%
	male	15	20%		18	45%		11	24%		5	22%
Race	white	69	93%	1.00	38	95%	1.00	44	98%	1.00	22	96%
	other	5	7%		2	5%		1	2%		1	4%
Smoking status	current	14	19%	0.77	11	28%	0.54	5	11%	0.66	4	17%
	former	24	32%		10	25%		15	33%		7	30%
	never	36	49%		19	48%		25	56%		12	52%
ASA class	1	23	31%	0.96	7	18%	0.12	18	40%	0.17	5	22%
	2	40	54%		23	58%		25	56%		17	74%
	3	10	14%		10	25%		2	4%		1	4%
	4	1	1%									
GERD	NO	54	73%	0.79	23	58%	0.11	22	49%	0.036	18	78%
	YES	20	27%		17	43%		23	51%		5	22%

\* Fisher exact test for Sex, Race, and GERD. Wilcoxon rank-sum test for Smoking and ASA class.

**Table 2b**  
: Patient demographics by group.

	Patient demographics by group										
	Biliary dyskinesia			Hyperdynamic gallbladder			Negative workup			Polyps	
	N	%	p-value* vs Polyps	N	%	p-value* vs Polyps	N	%	p-value* vs Polyps	Mean	Standard Deviation
AGE	45.0	14.9	0.042	44.0	15.8	0.047	41.8	14.5	0.0047	50.6	10.0
BMI	28.8	5.8	0.77	31.6	6.9	0.14	29.1	7.6	0.93	29.2	5.3

\* independent-samples *t*-test.

Table A.3

**Table 3**  
: Outcomes by diagnosis.

Group	Biliary dyskinesia	Short term outcome				Long term outcome			
		N	# success	% success	p-value vs. Polyps**	N	# success	% success	p-value vs. Polyps**
		Hyperdynamic gallbladder	40	36	90%	0.081	11	9	82%
Negative Workup	45	39	87%	0.11	7	4	57%	0.26	
Polyps	23	16	70%	—	9	8	89%	—	

\* "success" indicates fully or partially improved as opposed to not improved or worse.

\*\* Fisher exact test.

**Appendix B. Supplementary data**Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amjsurg.2019.03.017>.**References**

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