

**RESPONSE TO BILIARY SPHINCTEROTOMY IN PATIENTS WITH RUQ ABDOMINAL PAIN
FOLLOWING CHOLECYSTECTOMY**

A thesis submitted to the University of Arizona College of Medicine – Phoenix
in partial fulfillment of the requirements for the Degree of Doctor of Medicine

Chirag Kapadia
Class of 2020

Mentor: Teodor Pitea, MD

**Response to biliary sphincterotomy in patients with RUQ abdominal pain following
cholecystectomy**

Chirag Kapadia

Class of 2020

Mentor: Teodor Pitea, MD

Acknowledgements

I would like to thank my mentor, Dr. Teodor Pitea, as well as his fellow, Dr. Anam Omer, for the opportunity to be a part of this project. Furthermore, I would like to thank Paul Kang for his help through the statistical analysis on this project.

Abstract

Functional abdominal pain in post-cholecystectomy patients is often related to visceral hypersensitivity (VH) and can have a lasting impact on a patient's wellbeing. Numerous factors may lead to persistent or recurrent abdominal pain in post-cholecystectomy patients, one such factor may be Sphincter of Oddi Dysfunction (SOD) or papillary stenosis. Many patients undergo biliary sphincterotomies to achieve symptomatic resolution. This study observed 49 patients stratified by demographic information (age, gender, race, BMI, and inpatient status). It was determined that patients complaining of biliary pain post-cholecystectomy with failure to respond to medical management papillary stenosis and SOD should be considered. For these patients, symptom improvement was observed in 93%. An association was also seen with symptomatic resolution stratified for demographic data exemplifying that male patients, non-Caucasian patients and patients with in-patient status were more likely to achieve symptomatic improvement and resolution. Although a statistical significance was not observed for symptomatic resolution, it can be said that certain people will be more likely to experience resolution with a sphincterotomy than others.

Introduction

Functional abdominal pain is often related to visceral hypersensitivity (VH) in patient's post-cholecystectomy and can have a lasting impact on a patient's wellbeing. Patients often fail medical management and witness symptomatic relapse. The patients are commonly referred for evaluation of Sphincter of Oddi dysfunction (SOD) and papillary stenosis, and further treated with biliary sphincterotomies in hopes of symptom resolution. Even still, there persists the issue of patients unable to achieve symptomatic resolution, and, even with sphincterotomy, some patients will experience symptom recurrence (1).

Sphincter of Oddi Dysfunction

The sphincter of Oddi consists of smooth muscle that contracts to block biliary flow. Consisting of three sphincteric regions, the sphincter of Oddi has a biliary sphincter to control the common bile duct (CBD) flow, a pancreatic sphincter to control the pancreatic duct (PD) flow, and common sphincter proximal to the duodenum where an outlet exists, the Ampulla of Vater (6).

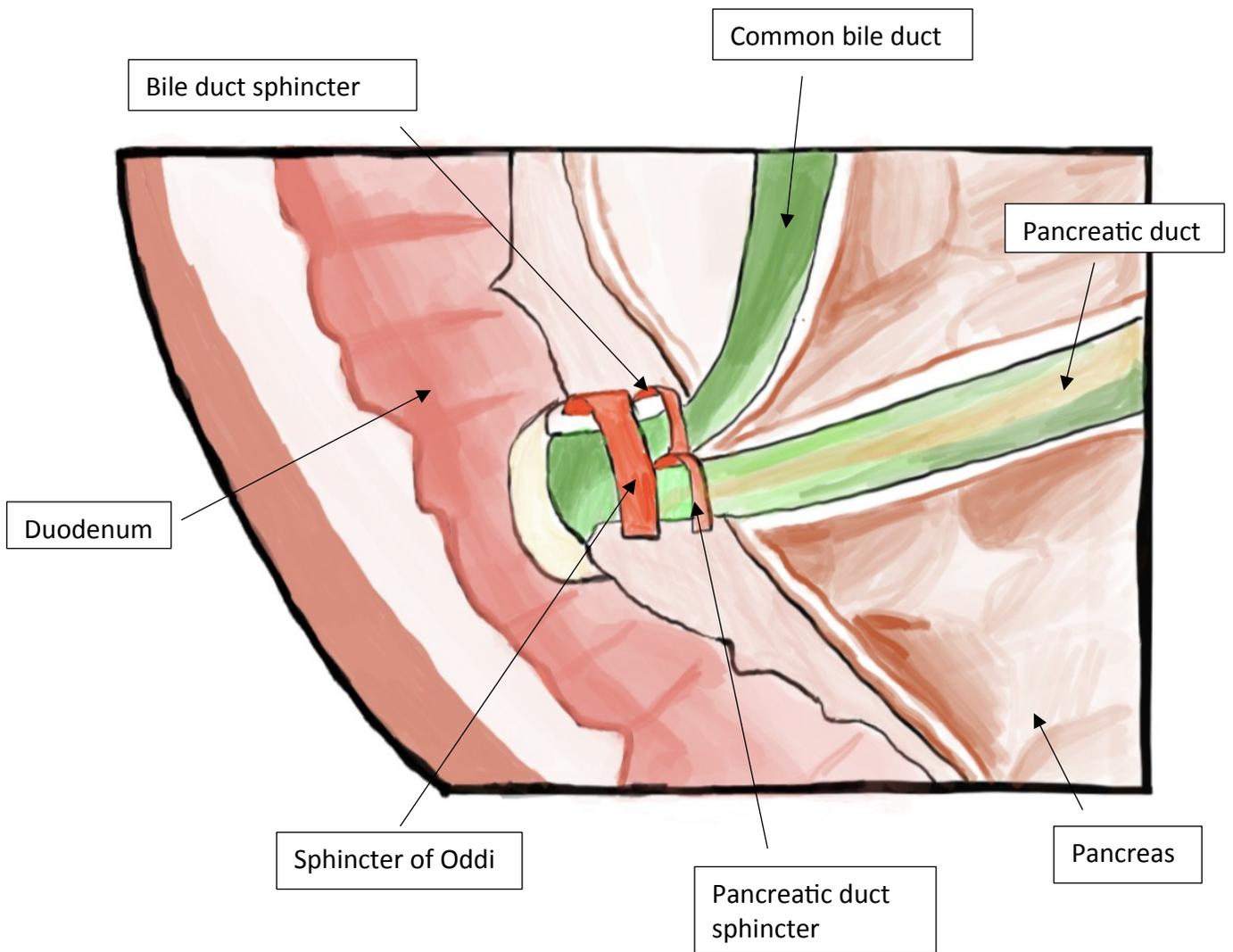


Figure #1: Sphincter of Oddi and anatomic relationships. Taken with permission from illustrator

Varun P. Sharma⁹

During a sphincterotomy, a portion of the intraluminal sphincter is transected. This procedure is often completed to help relieve SOD, thought to be pain caused by increased pressure from secretory backflow (3). Clinically, patients present with intermittent biliary pain described as a RUQ pain or epigastric pain with possible radiation to the back, scapula, or shoulder. The pain is often not associated with eating patterns and remains unrelieved from bowel movements, antacid usage or postural changes (6).

Although clinically the symptoms are similar, the etiology of Sphincter of Oddi dysfunction is unclear and it is thought to be caused by either a function issue (dyskinesia) or a mechanical obstruction (anatomic) that can be further classified as either pancreatic SO or biliary SO dysfunction (2). Moreover, Sphincter of Oddi dysfunction is defined by Pop as a structural or functional abnormality of the sphincter's motility that interferes with bile or pancreatic duct drainage (8). These classifications can be used to categorize three types of SOD: Type I with biliary-type pain, abnormal LFT's, dilated CBD, and delayed drainage; Type II with biliary pain and one or more of the previous characterizing features (abnormal LFT's, dilated CBD, and delayed drainage); Type III with biliary pain without other characterizing findings (11). It is difficult to distinguish biliary pain from gallbladder dysfunction from SOD, so it is often diagnosed after cholecystectomy. However, the presence of dilated CBD and elevated LFT's leads one to consider papillary stenosis as the cause of SOD. This has been further corroborated by other studies that have shown fibrosis and inflammation in ampullary biopsies of nearly 42% of patients with SOD (7).

Treatment options for SOD have traditionally included a sphincterotomy with or without manometry, and this has remained a mainstay for treatment in patients with papillary stenosis. Still, studies have observed symptom improvement after sphincterotomy, but relapse of patient symptoms is relatively common and can be seen in up to 32% of patient's after sphincterotomy according to some researchers (4).

Visceral Hypersensitivity

Visceral pain affects a plethora of patients, yet it remains an enigma as we endeavor to close the knowledge gap regarding the mechanisms through which we feel this chronic pain.

Functional gastrointestinal disorders (FGID) would be an example of visceral pain, wherein there is no diagnostic clue to why the patient is suffering. Still, one article defines a key pathological factor in FGID as visceral hypersensitivity (VH). Although the mechanism remains unclear, it is hypothesized to be caused by a multitude of factors including “peripheral sensitization, central sensitization, aberrant central processing, genetic, psychological and abnormalities within the stress response system” (5). One example of an FGID would be irritable bowel syndrome (IBS), a syndrome in which it is not uncommon for patients to suffer through VH and chronic pain (10). Even after sphincterotomy, some patients do not see resolution of this visceral pain and may go on towards having chronic pain. Still there is not much data to support what characteristics a patient may have that may lead them towards higher chances of symptom resolution.

Rationale

Pain is not uncommon to patients suffering from SOD, and even after undergoing sphincterotomy, some patients do not experience long-term symptom resolution. This pain can become debilitating and lead to the need of long-term management and care. With this in mind, *the study aims to assess the symptom management after endoscopic sphincterotomy in a subgroup of patients with post-cholecystectomy right upper quadrant pain. Furthermore, the patient data is stratified according to demographic data (age, gender, race, BMI and inpatient status) to observe difference in symptom management between patient differentiators.*

Methods

This study is a retrospective review from 2015 to 2018 observing treatment outcomes of patients who are post-cholecystectomy with right-upper quadrant (RUQ) abdominal pain refractory to treatment. Each patient had undergone biliary sphincterotomy by single endoscopist. Exclusion criteria included patients with pancreaticobiliary malignancies or prior history of pancreatitis. Records were obtained through electronic medical records available through the timeline intervals. Over 400 charts were screened to exclude patients without hypersensitivity post-procedure. 49 patient charts were included in the study, and each patient chart was reviewed, and de-identified information was collected. Data collection included patient demographic information (age, DOB, gender, BMI, ethnicity), clinical symptoms before and after ERCP, elevated liver functions tests, common bile duct size, narcotic use, prior history of IBS, procedure complications (post including pancreatitis and bleeding) and pancreatic duct stent placement. Patient response to procedure and symptom resolution were also collected as well as length of stay during admission and pharmacological treatment. Statistical analysis was completed by Paul Kang through simple descriptive statistics, proportions and percentages. The study sponsor was Banner- University Medical Center Phoenix and the study received approval from Banner Health IRB- Phoenix Panel.

Results

A total of 49 patients were included in the study. Mean age was found to be 54.9 years with 5 males and 44 females. 7 patients were identified to be non-Caucasian patient. 44 patients (89.8%) were found to have constant RUQ pain. 38 patients (77.5%) were found to have a dilated CBD and 6 patients (12.2%) were found to have elevated LFT's. Of the patient population 2 (4.1%) had minor complications including pain and mild pancreatitis and 1 patient (2%) had a major complication (necrotizing pancreatitis). 26 patients (53%) had prophylactic pancreatic duct stent placed and 29 patients (59.1%) were discharged home after the procedure.

The following data tables relay the information discovered in the study:

Variables	Overall N=49	No Improvement N=3	Improvement only N=35	Resolved N=11	p-value
Age, years (median, IQR)	54.9 (45.4, 65.9)	66.5 (27.2, 70.3)	52.6 (44.3, 60.2)	55.8 (45.4, 71.4)	0.66
Gender (male, %)	5 (10.2)	0 (0.0)	3 (8.57)	2 (18.2)	0.70
Race (non-Caucasian, %)	7 (14.3)	0 (0.0)	4 (11.4)	3 (27.3)	0.46
BMI, kg/m ² (median, IQR)	27.2 (23.5, 29.1)	27.2 (25.8, 28.6)	27.2 (23.5, 29.7)	25.1 (19.1, 29.1)	0.49
Inpatient (yes, %)	6 (12.2)	0 (0.0)	3 (8.57)	3 (27.3)	0.30

Table #1: Symptom management post-sphincterotomy stratified by demographic data

Table #1 conveys that out of the 49 patients, a total of 46 patients (93.8%) reported symptom improvement post-sphincterotomy. Of those, 35 patients (71.4%) reported partial resolution while 11 patients (22.4%) reported complete symptom resolution. 3 patients (6%) showed no improvement at all after the procedure.

Variables	No Improvement N=3	Improvement or resolved N=46	p-value
Age, years (median, IQR)	66.5 (27.2, 70.3)	54.9 (45.4, 64.6)	0.86
Gender (male, %)	0 (0.0)	5 (10.8)	1.0
Race (non-Caucasian, %)	0 (0.0)	7 (15.2)	1.0
BMI, kg/m ² (median, IQR)	27.2 (25.8, 28.6)	27.2 (23.4, 29.3)	0.72
Inpatient (yes, %)	0 (0.0)	6 (13.0)	1.0

Table #2: No improvement vs. symptom improvement

Variables	No Improvement or Improved N=38	Resolved N=11	Or (95% CI)	p-value
Age, years (median, IQR)	53.7 (44.4)	55.8 (45.4, 71.4)	1.96 (0.41, 9.23)	0.82
Gender (male, %)	3 (7.89)	2 (18.2)	2.17 (0.16, 29.7)	0.79
Race (non-Caucasian, %)	4 (10.5)	3 (27.3)	2.54 (0.38, 16.9)	0.22
BMI, kg/m ² (median, IQR)	27.2 (23.9, 29.3)	25.1 (19.1, 29.1)	0.50 (0.11, 2.28)	0.37
Inpatient (yes, %)	3 (27.3)	3 (27.3)	5.04 (0.68, 37.5)	0.11

Table #3: No improvement and improvement vs. symptom resolution

Tables #2 and #3 convey that there were no differences observed between demographic values and combination of post-procedure responses.

Discussion

Patients suffering from Sphincter of Oddi dysfunction and biliary stenosis endure right upper quadrant pain that can become unrelentless. Often times these patients undergo biliary sphincterotomy, but still the pain may persist. Furthermore, a subset of these patients do not experience long-term symptomatic resolution although they may find symptomatic improvement. This study aimed to assess this symptomatic management after endoscopic sphincterotomy in a subgroup of patients with post-cholecystectomy RUQ pain. Furthermore, the patient data in this study was stratified according to demographic data (age, gender, race, BMI and inpatient status) to observe differences in symptomatic management between patient differentiators.

The majority (71%) of patients were observed to have had symptom improvement after the biliary sphincterotomy. Of the patient population in whole, 22% were seen to have achieved complete symptomatic resolution. Still, there was no tangible association appreciated in regard to patient demographic values and post-procedure responses. However, two trends were observed although they were not found to be associated with statistical significance. One was that symptom improvement or resolution was more likely to be observed in males and the other that this same trend was observed in patients that had in-patient status being admitted to the hospital post-procedure.

The above tables also relay odd's ratios for the various stratifications. These OR's described that patients with an increased BMI (>25) were less likely to see symptomatic resolution and the odds of symptomatic resolution therefore decreased. Inversely, patients that were noted to be aged greater than the media, patients that were male, and patients that were non-Caucasians

were more likely to observe symptomatic resolution. For these patients, the odds were increased that they would experience symptom resolution. Finally, patients that remained in-patient post-procedure were observed to have had the highest increase in probability towards achieving symptomatic resolution.

Conclusion

In patients complaining of biliary pain post-cholecystectomy with failure to respond to medical management, papillary stenosis and SOD should be considered. For these patients, at least some symptom improvement was seen in 93% of cases reviewed. Moreover, it can be said that there is an underlying association towards achieving symptomatic resolution when stratifying for demographic data. Although a statistical significance was not observed for symptomatic resolution, it can be said that certain people will be more likely to experience resolution with a sphincterotomy than others.

Limitations existed within this study. Confounding variables included concurrent medication usage including narcotics, SSRI's, SNRI's and other medication classes. Limitations also existed on chart availability and patient follow-up post-procedure. Future directions for this study include addressing concurrent medication usage as an additional factor when considering symptomatic improvement and resolution. Additionally, future studies may be able to look at utilizing new medical and pharmacological treatments aimed at improving complete symptomatic resolution in patients that have undergone sphincterotomies.

References:

1. Afghani, E., Lo, S. K., Covington, P. S., Cash, B. D., & Pandol, S. J. (2017). Sphincter of Oddi Function and Risk Factors for Dysfunction. *Frontiers in nutrition*, 4, 1. doi:10.3389/fnut.2017.00001
2. Behar, J., Corazziari, E., Guelrud, M., Hogan, W., Sherman, S., & Toouli, J. (2006). Functional gallbladder and sphincter of Oddi disorders. *Gastroenterology*, 5, 130, 1498-1509. doi: 10.1053/j.gastro.2005.11.063
3. Bistriz, L., & Bain, V. G. (2006). Sphincter of Oddi dysfunction: managing the patient with chronic biliary pain. *World journal of gastroenterology*, 12(24), 3793–3802. doi:10.3748/wjg.v12.i24.3793
4. Claude, A., Jean-Bernard, F., Jean-François, D. (2000). Ampulla of Vater: anatomic, embryologic, and surgical aspects. *Surgical Clinics of North America*, 80, 1, 201-12. Doi:10.1016/S0039-6109(05)70402-3
5. Farmer, A. D., & Aziz, Q. (2013). Gut pain & visceral hypersensitivity. *British journal of pain*, 7(1), 39–47. doi:10.1177/2049463713479229
6. Miyatani, H., Mashima, H., Sekine, M., & Matsumoto, S. (2019). Clinical course of biliary-type sphincter of Oddi dysfunction: endoscopic sphincterotomy and functional dyspepsia as affecting factors. *Therapeutic advances in gastrointestinal endoscopy*, 12, 2631774519867184. doi:10.1177/2631774519867184
7. Ponchon, T., Aucia, N., Mitchell, R., Chavaillon, A., Bory, R., & Hedelius, F. (1995) Biopsies of the ampullary region in patients suspected to have sphincter of Oddi dysfunction. *Gastrointestinal Endoscopy*, 42, 4, 296-300. doi: 10.1016/S0016-5107(95)70125-7
8. Pop, C., Purcăreanu, A., Purcărea, M., & Andronescu, D. (2008). The functional sphincter of Oddi disorder. *Journal of medicine and life*, 1(2), 118–129.

9. Sharma, V. (2020) "Sphincter of oddi dysfunction and anatomic relationships".
10. Thoua, N & Murray, Charles & Winchester, Wendy & Roy, AJ & Pitcher, M & Kamm, MA & Emmanuel, AV. (2008). Amitriptyline modifies the visceral hypersensitivity response to acute stress in the irritable bowel syndrome. *Alimentary pharmacology & therapeutics*. 29. 552-60. [10.1111/j.1365-2036.2008.03918.x](https://doi.org/10.1111/j.1365-2036.2008.03918.x).
11. Wilcox, C. (2015) Sphincter of oddi dysfunction Type III: New studies suggest new approaches are needed. *World journal of gastroenterology*, 21(9), 5755-5761.
[doi:10.3748/wjg.v21.i19.5755](https://doi.org/10.3748/wjg.v21.i19.5755)