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Research Paper

Mirizzi syndrome: The Trojan horse of gallbladder disease

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ABSTRACT

Background: The incidence of Mirizzi Syndrome ranges from 0.05 to 5.7 % of patients who undergo cholecystectomy. The purpose of this study is to examine the preoperative workup and postoperative outcomes for patients diagnosed with Mirizzi Syndrome.
Methods: Retrospective chart review was conducted between January 2018 and January 2022 at a single institution. All adult patients who underwent cholecystectomy were included.
Results: 1628 patients underwent cholecystectomy of which 47 were diagnosed with Mirizzi Syndrome. The majority of patients had type 1 Mirizzi Syndrome. Preoperative studies were often nondiagnostic and 81 % of cases were diagnosed intraoperatively. 66 % of cases were performed laparoscopically, an open approach was required for type V Mirizzi Syndrome. The complication rate was 25 %; most commonly a bile leak requiring ERCP.
Conclusion: Mirizzi syndrome is more common than previously expected and related to patient's ability to seek timely medical care. Most cases can be completed laparoscopically however there is a high rate of complications.
Key message: This study presents an additional cohort of patients found to have Mirizzi syndrome and supports the hypothesis that it is difficult to diagnose preoperatively. Cases should be attempted laparoscopically but there remains a high complication rate.

Introduction

Mirizzi syndrome describes chronic symptomatic gallstone disease, resulting in external compression of the common bile duct or hepatic duct [1–6]. Common clinical manifestations include right upper quadrant pain, fever, and obstructive jaundice. Studies indicate that Mirizzi Syndrome occurs in 0.05–2.1 % of patients who receive cholecystectomies in developed countries and between 4.7–5.7 % in developing countries [7–9]. The severity of disease is linked to the chronicity of symptoms with repeat episodes of acute cholecystitis leading to gallbladder fibrosis, contracture, fistula formation and increased surgical complications.

The preoperative workup includes various imaging modalities, each exibiting low diagnostic accuracy: ultrasound – 30 %, CT – 42 %, MRCP – 50 %, ERCP – 63 % [9–14]. Intraoperatively, dense adhesions of the porta hepatis and contracted gallbladders are common signs of a Mirizzi pathology. The level of inflammation and frequent anatomic variations can make intraoperative cholangiograms, which can help delineate the anatomy, more difficult to perform [15–17]. This study aims to access the incidence of Mirizzi Syndrome beyond previous reports, examining hospital courses and surgical outcomes to enhance preoperative planning and intervention recommendations.

Materials and methods

A retrospective chart review was conducted of all cholecystectomies performed between January 2018 and January 2022 at a single institution. Exclusion criteria included age <18 years old. Patient demographics including diagnosis, imaging, laboratory values, procedures and operative reports were reviewed. All those with choledocholithiasis proven by ERCP, MRCP, and/or IOC and those with gallbladder malignancy were excluded. Mirizzi syndrome was defined as obstruction of the common hepatic duct or common bile duct secondary to compression from a gallstone in the infundibulum or cystic duct. Patients' charts that met these criteria were then analyzed for details of care including number of prior emergency room visits and diagnosis, preoperative

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evaluation, and intervention with suspicion of Mirizzi syndrome, operative management, and subsequent length of stay (LOS), and associated complications.

Mirizzi Syndrome was classified in Types I through V. Type I describes compression of the bile duct due to impaction from a single or multiple stones in the cystic duct or Hartmann's pouch. Type II delineates a fistula between the gallbladder and bile duct due to erosion of their walls from the calculus. This fistula is less than one-third of the bile duct circumference. Type III describes a fistula that involves two-third of the circumference of the bile duct. Type IV describes complete fusion of the gallbladder to the bile duct due to fistula formation. Type V represents the development of a cholecystoenteric fistula, with Type Va excluding gallstone ileus and Type Vb including the complication of gallstone ileus.

This study was approved by the Institutional Review Boards at both the University Medical Center (Las Vegas, NV) and Kirk Kerkorian School of Medicine at UNLV. Categorical clinical variables were summarized using counts and percentages. The median and interquartile ranges were recorded for continuous variables. Student's *t*-test and ANOVA testing was performed for quantitative variables while Fisher Exact test was used for qualitative variables. An alpha level of 0.05 was used for all significance testing. All statistics were performed on SPSS Statistics 28 (IBM Corp., Armonk, New York).

Results

Over four years, 1628 patients underwent cholecystectomy of which 47 patients met inclusion criteria for Mirizzi syndrome. There was a similar number of males and females (Table 1). The mean age was 53 years old (range 20–85). The highest race/ethnicity was white, Hispanic patients ($N = 26$, 53.3 %) and the lowest incidence was in non-white patients ($N = 7$, 14.9 %). Seventy percent of people had Medicare or Medicaid compared to private insurance. The most common type of Mirizzi was type 1 ($N = 35$) and least common was type 4 ($N = 0$).

Table 1
Patient characteristics by type of Mirizzi.

	Overall	1	2	3	4	5	p
N, (%)	47	35 (74.4)	5 (10.6)	1 (0.2)	0 (0)	6 (12.8)	–
Age, mean, (SD)	53.6 (15.7)	53.4 (15.6)	51.0 (22.9)	48.0 (–)	0 (0)	58.0 (12.3)	0.87
Age group, n, (%)							
<65y	36 (76.5)	28 (77.8)	3 (8.3)	1 (2.8)	0 (0)	4 (11.1)	0.65
>65y	11 (23.5)	7 (63.6)	2 (18.2)	0 (0)	0 (0)	2 (18.2)	
Sex, n, (%)							
Male	25 (53.2)	20 (80.0)	3 (12.0)	1 (4.0)	0 (0)	1 (4.0)	0.22
Female	22 (46.8)	15 (68.2)	2 (9.1)	5 (22.7)	0 (0)	5 (22.8)	
Race/ ethnicity, n, (%)							
White, Hispanic	26 (55.3)	21 (80.8)	3 (11.5)	0 (0)	0 (0)	2 (7.7)	0.27
White, non-Hispanic	14 (29.8)	8 (57.1)	1 (7.1)	1 (7.1)	0 (0)	4 (28.6)	
Non-white	7 (14.9)	6 (85.7)	1 (14.3)	0 (0)	0 (0)	0 (0)	
Type of insurance, n, (%)							
Private	14 (29.8)	10 (71.4)	1 (7.1)	1 (7.1)	0 (0)	2 (14.3)	0.44
Public	33 (70.2)	25 (75.8)	4 (12.1)	0 (0)	0 (0)	4 (12.1)	

Preoperative bilirubin was similar between all types of Mirizzi (Table 2). Patients with Mirizzi syndrome did not have a high incidence of elevated lipase (8.5 %) but did have transaminitis (63.8 %). More than half of patients (53 %) underwent an MRCP but when performed it was suspicious for Mirizzi in only 24 % of cases. A smaller number of patients (28 %) underwent ERCP and it was suspicious for this syndrome in 38 % of cases. 45 (95.7 %) patients were seen in the ER for a prior episode of right upper quadrant pain. Of those patients, 6 (13.3 %) were previously diagnosed with choledocholithiasis. Only 1 patient (2.1 %) was admitted for elective cholecystectomy and the others (97.8 %) were admitted through the emergency room for urgent surgery.

There were multiple preoperative workups with various combinations of lab work and imaging. Based on those workups, only 2 cases of Mirizzi syndrome were identified preoperatively; one was a Type II and the other was a Type V. Both of these patients underwent US and MRCP but the diagnosis was not made until an ERCP was performed. 81 % of the cases of Mirizzi were diagnosed intraoperatively ($N = 38$). An intraoperative cholangiogram was performed in 32 % of cases with most of the Type V cases (67 %) undergoing IOC. The most common surgical approach was laparoscopic (66 %). Conversion from laparoscopic to open surgery was most frequent for Type V Mirizzi (83.3 %) compared to Type I Mirizzi (17.1 %) ($p = 0.05$). One case of Type V Mirizzi was completed through an open approach from the start.

Postoperatively, the mean length of stay was 6 days (Range 0–33 days). The hospital stay was longest for Type V and shortest for Type I ($N = 10$ days, $N = 5$ days respectively). Of the cases, 25 % had a complication. This was highest for Type V Mirizzi (67 %) ($p = 0.05$). Stenosis requiring a stent occurred in 2 patients (16 %) both of whom underwent original surgeries totally laparoscopic. A biliary leak requiring stent placement occurred in 5 patients (41 %). There were 4 infectious complications (33 %), 2 patients developed pancreatitis and 2 other patients developed an abscess (Tables 3 to 5).

Discussion

Mirizzi syndrome poses diagnostic challenges. Preoperative imagining is often nonspecific and relies on intraoperative diagnosis. Despite this, the majority of cases can be undertaken laparoscopically with good clinical outcomes [10,15]. This study examines the workup, management and outcomes of patients diagnosed with Mirizzi Syndrome at a county teaching hospital.

Mirizzi syndrome pathophysiology reflects chronic changes of untreated cholelithiasis. It is reported in 0.05 to 2.1 % of patients who

Table 2
Preoperative workup by type of Mirizzi grouped.

	Overall	1	2,3,4	5	p
N, (%)	47	35 (74.4)	6 (12.8)	6 (12.8)	–
Bilirubin, n, (%)					
<2	22(46.8)	16 (45.7)	2 (33.3)	4 (66.7)	0.17
>2	24 (51.0)	18 (51.4)	4 (66.7)	2 (33.3)	
Unmeasured	1 (2.1)	1 (2.9)	0 (0)	0 (0)	
Transaminitis, n, (%)					
No	15 (31.9)	9 (25.7)	2 (33.3)	4 (66.7)	0.50
Yes	30 (63.8)	24 (68.6)	4 (66.7)	2 (33.3)	
Unmeasured	2 (4.3)	2 (5.7)	0 (0)	0 (0)	
Lipase, n, (%)					
<234	42 (89.4)	31 (88.6)	5 (83.3)	6 (100)	0.59
>234	4 (8.5)	3 (8.6)	1 (16.7)	0 (0)	
Unmeasured	1 (2.1)	1 (2.8)	0 (0)	0 (0)	
MRCP, n, (%)					
Consistent with Mirizzi	6 (12.8)	4 (11.4)	2 (33.3)	0 (0)	0.50
Other findings	19 (40.4)	14 (40.0)	3 (50.0)	2 (33.3)	
Not performed	22 (46.8)	17 (48.6)	1 (16.7)	4 (66.7)	
ERCP, n, (%)					
Consistent with Mirizzi	5 (10.6)	2 (5.7)	1 (16.7)	2 (33.3)	0.51
Other findings	8 (17.0)	5 (14.3)	2 (33.3)	1 (16.7)	
Not performed	34 (72.4)	28 (80.0)	3 (50.0)	3 (50.0)	

Table 3
Intraoperative findings by type of Mirizzi grouped.

	Overall	1	2,3,4	5	p
N, (%)	47	35 (74.4)	6 (12.8)	6 (12.8)	–
Mirizzi diagnosed, n, (%)					
Preoperative	2 (4.2)	0 (0)	1 (16.7)	1 (16.7)	0.13
Intra-operative	38 (80.9)	29 (82.9)	5 (83.3)	4 (66.7)	
Other	7 (14.9)	6 (17.1)	0 (0)	1 (16.6)	
IOC, n, (%)					
Performed	15 (31.9)	9 (25.7)	2 (33.3)	4 (66.7)	0.50
Not performed	30 (63.8)	24 (68.6)	4 (66.7)	2 (33.3)	
Operative approach, n, (%)					
Stayed laparoscopic	31 (66.0)	29 (82.9)	2 (33.3)	0 (0)	0.01
Laparoscopic to open	15 (31.9)	6 (17.1)	4 (66.7)	5 (83.3)	
Stayed open	1 (2.1)	0 (0)	0 (0)	1 (16.7)	

Table 4
Postoperative course by type of Mirizzi grouped.

	Overall	1	2,3,4	5	p
N, (%)	47	35 (74.4)	6 (12.8)	6 (12.8)	–
Complication, n, (%)					
Yes	12 (25.5)	7 (20.0)	1 (16.7)	4 (66.7)	0.04
No	35 (74.5)	28 (80.0)	5 (83.3)	2 (33.3)	
LOS, n, (SD)	6 (6.2)	5 (5.4)	7.8 (4.5)	10 (10.25)	0.14

receive cholecystectomies in developed countries. The rate reported in developing countries is between 4.7–5.7 % [7–9]. The disparity is attributed to access and patient's social determinants of health. In this study, the rate was found to be 2.8 % which was higher than expected. A study by Ambur et al. showed that patients with Medicare or Medicaid who have gallbladder pathology are less likely to undergo elective surgery [18]. Medicaid expansion in our state brought about robust access to healthcare services. Despite this, patients did not undergo elective cholecystectomy after being seen in the ER. Instead, patients present later in their pathology with more advanced disease. To combat this, efforts should focus on improving outpatient follow up among our population.

Workup varied among patients but included a combination of lab work and preoperative ERCP and/or MRCP. Lab workup showed total bilirubin and lipase was not indicative of Mirizzi Syndrome. Unlike in choledocholithiasis, obstruction of the bile duct is intermittent, and the pancreatic duct is not usually affected. Imaging studies were also infrequently suggestive of Mirizzi syndrome with the majority of patients receiving the diagnosis intraoperatively. Retrospective review of this imaging could confirm preoperative suspicion in only some cases, all of them type 1,2, or 3. In the event of a type 5, the relationship between the gallbladder and another organ could be on CT but this was unlikely to precipitate ERCP or MRCP therefore the fistula wasn't known preoperatively. The unique imaging features seen in Mirizzi syndrome can be difficult to discern in practice which restricts the ability for preoperative planning. Limitations in imaging suggest surgeons maintain a high level of suspicion during the operation to diagnose patients intraoperatively [15–17].

As laparoscopists become more advanced, the treatment of Mirzzi Syndrome has also evolved. Studies have shown that those treated with a laparoscopic approach have better outcomes with less intraoperative blood loss and lower length of stay while maintaining a similar complication rate [19,20]. This study finds the laparoscopic approach successful for type I through IV while those with type V required conversion to open. Patients who follow a clinical picture of Mirizzi, even with inconclusive preoperative imaging, should be attempted laparoscopically. This has been supported in the literature with case reports

Table 5
Details of intraoperative and postoperative management.

Type of Mirizzi	Intraoperative drain	Notes	Complication (Y/N)
1	–	–	N
1	19Fr	Kept at time of discharge, POD2	N
1	19Fr	Drain removed POD1	N
1	–	–	N
1	–	–	N
1	–	–	N
1	–	–	N
1	–	–	N
1	–	–	N
1	–	–	N
1	–	–	N
1	19Fr	Drain removed POD4	N
1	–	–	N
1	–	–	N
1	–	–	N
1	–	–	N
1	–	–	N
1	–	–	N
1	19Fr	Kept at time of discharge, POD4	N
1	–	–	N
1	–	–	N
1	–	–	N
1	19Fr	Drain removed POD3	N
1	7Fr	Drain removed POD2	N
1	–	–	N
1	–	–	N
1	–	–	Y
1	7Fr	Drain removed POD3	Y
1	19Fr	Drain removed POD6	Y
1	–	–	Y
1	19Fr	Kept at time of discharge, POD3	Y
1	–	–	Y
1	19Fr	Kept at time of discharge, POD2	Y
2	19Fr	Drain removed POD3	N
2	–	–	N
2	–	–	N
2	–	–	N
2	19Fr	Drain removed POD4	Y
3	T tube, 10Fr	Kept at time of discharge, POD5	N
5	–	–	N
5	–	–	N
5	–	–	Y
5	10Fr	Drain removed on POD5	Y
5	12Fr	Kept at time of discharge, POD3	Y
5	12Fr	Kept at time of discharge, POD3	Y

by Jimenez et al. and T-Y et al. which detailed success with ERCP guided therapy followed by laparoscopic surgery [21,22]. We argue for an increased use of endoscopic adjuncts preoperatively in the case that may involve Mirizzi pathology.

The complication rate of this study was consistent with the literature [15–17]. Historically, the majority of complications were seen after a procedure on type V Mirizzi syndrome [23]. This trend was noted in our study. Given the high incidence of bile leaks, we recommend routine drain placement in all patients and postoperative ERCP for patients with a type V Mirizzi. Postoperative discussions should focus on counseling including the high incidence of complications and symptoms of concern.

Limitations of the study include its retrospective nature. Although it is a single center study, this allows for a uniform surgical technique and management which is a deficit of similar studies [19,20,23]. Future studies should examine the impact of a robotic platform on laparoscopic outcomes for Mirizzi patients.

Conclusions

Mirizzi syndrome may not be as rare as previously reported. It should be suspected in patients who repeatedly present with symptomatic cholelithiasis and their surgery should be prioritized. The lab workup is of variable importance, but a high index of suspicion should remain to improve preoperative diagnosis. The majority can be performed laparoscopically but conversations should focus on the high incidence of complications.

Ethical approval statement

This study was approved by the University Medical Center Institutional Review Board: UMC-2021-400.

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CRediT authorship contribution statement

Mary Froehlich: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Elizabeth M. Sodomin:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Taylor Fontenot:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Noama Iftekhar:** Formal analysis, Investigation, Methodology, Writing – original draft. **Christian N. Chan:** Methodology, Project administration, Supervision. **Annabel Barber:** Conceptualization, Data curation, Formal analysis, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

There are no conflicts of interest to report.

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