



**ORIGINAL RESEARCH PAPER**

**General Surgery**

**CURRENT TRENDS IN THE MANAGEMENT OF MIRIZZI SYNDROME**

**KEY WORDS:** endoscopic, laparoscopic, Mirizzi Syndrome

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**ABSTRACT**

Mirizzi Syndrome is a rare and challenging clinical entity to manage. However, recent advances in technology have provided surgeons with new options for more effective diagnosis and treatment of this condition. This article reviews these new diagnostic modalities and treatment approaches for the management of Mirizzi Syndrome. This study was done on patients admitted in L.G. Hospital surgical wards, Ahmedabad with diagnosis of acute cholecystitis and cholelithiasis from 2018 to 2020. An active search of Mirizzi Syndrome in those patients was done by using further diagnostic techniques. In total 10 cases, 7 case reports were identified and analysed. The most frequently used diagnostic modalities were ultrasound, computed tomography (CT); magnetic resonance cholangiopancreatography (MRCP); endoscopic retrograde cholangiopancreatography (ERCP). A combination of >2 diagnostic modalities was frequently used to detect Mirizzi Syndrome. Article shows that the specific type of Mirizzi Syndrome determined the type of treatment chosen. Open surgery was the preferred option, although there are documented cases of the use of minimally invasive techniques, even in advanced cases. Laparoscopic, endoscopic or robot assisted surgery, used individually or in combination with lithotripsy, are all associated with a favourable outcome. As yet, there are no internationally accepted guidelines for the management of Mirizzi Syndrome. Laparotomy is the preferred surgical technique of choice, although an increasing number of surgeons are beginning to opt for minimally invasive techniques. The number of papers in the existing literature describing diagnostic and treatment procedures is relatively small at present, thus making it difficult to reasonably propose an evidence based standard of care for Mirizzi Syndrome.

**INTRODUCTION**

Mirizzi Syndrome was first described by Kehr and Ruge in 1905, they published was of biliary obstruction by gall bladder stone. Pablo Mirizzi (1893-1963) a surgeon in Corodoba, Argentina had first described and analysed external compression of biliary duct by stone in Gall bladder and Common bile duct and leading to operative complication and then this condition was named Mirizzi Syndrome.

It is a condition in which there is an external compression due to single or multiple impacted stones in cystic duct and Hartmann's pouch leading to dilatation in a proximal duct which leads to pressure necrosis of CBD, which leads to fistula formation. Mirizzi Syndrome is one of the rare disorder resulting in chronic inflammation and ulceration from varying degrees of cholecystobiliary fistula. Furthermore, cholecystoenteric fistula may also occur, which can leads to obstruction too.

According to pathophysiological features, Mirizzi Syndrome can be classified into several different types (Table 1). Mirizzi Syndrome is detected in 0.06% to 5.7% of patients during cholecystectomy, and in 1.07% of patients undergoing endoscopic retrograde cholangiopancreatography (ERCP). [4,11,12]. Anatomical predispositions include side-by-side location of the cystic and common hepatic ducts, coupled with a long, low inserting cystic duct to the biliary tree. Beltrán[8] observed 9 anatomical elements associated with Mirizzi Syndrome. First, an atrophic gallbladder with either thick or thin walls, with impacted gallstones at the infundibulum or at the Hartmann's pouch, occasionally found firmly attached to the gallbladder wall.

Second, an obliterated cystic duct; which tends to represent a common finding. Third, a long cystic duct running parallel to the common bile duct with low insertion; this has been described as a risk factor for Mirizzi Syndrome. Fourth, a normal but short cystic duct. Fifth, partial obstruction by external compression of the bile duct or by a gallstone eroding into the bile duct originating from the gallbladder. Sixth, a normal caliber distal bile duct with walls of normal thickness. Seventh, a dilated proximal bile duct with thick inflamed walls. Eighth, an anomalous communication between the gallbladder and the bile duct. Finally, anomalous communication between the gallbladder and the stomach, duodenum, colon, or other abdominal viscera. Post-cholecystectomy residual cystic duct stones have also been implicated in Mirizzi Syndrome [13,14]. The clinical presentation of Mirizzi Syndrome ranges from asymptomatic to non-specific symptoms, with obstructive jaundice (27.8–100%) being the most common, elevated liver enzymes (AST/ALT), right upper quadrant abdominal pain (16.7–100%), and constitutional symptoms such as fever, nausea, vomiting, diarrhea, and constipation. Although rare, Mirizzi Syndrome may also present with gallstone ileus. [11]

The nature of these presentations often leads to this condition being confused with biliary tract neoplasm [15] and misdiagnosis is therefore common. The purpose of this article was to review existing literature relating to the diagnosis and treatment of Mirizzi Syndrome published within the last 5 years and to discuss the feasibility of new approaches in the management of Mirizzi Syndrome.

**METHODS**



associated laparoscopic treatment for Mirizzi Syndrome with low success rates; consequently, these authors did not recommend this technique. Despite these setbacks, minimally-invasive techniques in the management of Mirizzi Syndrome continue to be explored, albeit with limited application. Some treatment modalities, such as endoscopic and robotic-assisted techniques, are beginning to show preference with some authors.

**DISCUSSION**

**Classification Of Mirizzi Syndrome**

McSherry et al[5] described 2 types of Mirizzi Syndrome (Types I & II) based on ERCP findings of fistula formation. Type I includes evidence of gallstones impacting upon the Hartmann pouch or cystic duct along with slight external compression on the common bile duct (CBD). Cases of Type II show corrosion of the calculus into the CBD, along with cholecystobiliary fistula.

McSherry's classification of Type II was further redefined by Csendes et al[6] into 3 further types, based on the extent of erosion in the CBD circumference. Erosion involving less than one-third of the CBD circumference remained known as Type II, erosion up-to two-thirds the circumference of CBD became known as Type III, while Type IV involves complete destruction of the CBD wall. In 2008, Beltran et al[4] described an additional classification, Type V, as the presence of any of the first 4 types plus the formation of a cholecystoenteric fistula. Type V is further divided into Type Va (without gallstone ileus) and Type Vb (with gallstone ileus). However, other classifications also exist. Starling and Matallana[7] divided Type I into 2 subtypes: Ia (long cystic duct) and Ib (short cystic duct). In one study, Mirizzi Syndrome was present in 4 patients with acute acalculous cholecystitis. Opinion is divided as to whether these represent a separate class of the condition, or should be recognized as Type I. However, Beltrán[8] suggested that a simplified classification would be useful. In their classification, Mirizzi I corresponds to McSherry Mirizzi Type I while Mirizzi IIa and IIb have a cholecystobiliary fistula circumference less than half, and more than half of the CBD, respectively. Mirizzi Type III can have cholecystobiliary and cholecystoenteric fistula, thus Mirizzi IIIa without gallstone ileus and Mirizzi IIIb with. For further information on these classifications, refer to Table 1. For the purpose of this article, we have adhered to the classification proposed by Csendes. Our literature survey further showed that Mirizzi type I (10.5–51%)[4,21,26] and Mirizzi type II (57%) are the most commonly reported classifications.[17] Other types of Mirizzi Syndrome are relatively low in incidence.

**Diagnosis Of Mirizzi Syndrome**

Safe and effective surgical therapy is facilitated by accurate preoperative diagnosis. However, such diagnosis is often missed preoperatively, although more advanced cases of disease are easier to detect before surgery. In this article, we explore the following diagnostic modalities, which are all currently in use, including: abdominal ultrasonography; CT; MRCP, and ERCP.

**Abdominal US**

US is used as a routine investigation for biliary disease. This technique can reveal gallstones and cholecystitis and reveal evidence of Mirizzi Syndrome such as an atrophic gallbladder and ectatic common hepatic duct with a normal distal CBD, or edematous gallbladder caused by acute cholecystitis.[21] Existing literature confirms a diagnostic accuracy of 29%, with a sensitivity between 8.3% and 27%. [8,17,18,26] In one study involving 198 patients, the sensitivity of ultrasound for Mirizzi Syndrome was as high as 77.8%. [21]

**CT**

Although no specific radiological features of Mirizzi Syndrome can be recognized on CT imaging, this technique

can be very effective in detecting the cause and location of biliary obstruction.[8,16,19] CT is also useful for differentiating hepatic portal or hepatic infiltration of tumors.[42] In patients with cholecystobiliary fistula, CT scanning is valuable in distinguishing Mirizzi Syndrome from neoplasia. For example, Fabien et al[30] reported 5 cases in whom CT scan adequately diagnosed Mirizzi Syndrome, and concluded that adequate diagnosis can be reached on the basis of clinical symptoms and images on a CT scan.

**MRCP**

At present, MRCP is the preferred diagnostic tool, and is a non-invasive imaging technique with a 50% diagnostic accuracy rate. MRCP can delineate the typical characteristics of Mirizzi Syndrome, such as a stone in the common hepatic duct (CHD), extrinsic compression of the CHD, and dilatation of the CHD with normal-sized CBD. MRCP confirmation is required when ultrasound examination detects a dilated bile duct with evidence of obstructive jaundice or stone impaction in the bile duct. Biliary and pancreatic ducts can also be assessed by MRCP, which can create superior images of inflammation around the gallbladder. Such inflammation is characteristic of Mirizzi Syndrome, and can therefore be used to distinguish biliary conditions including cancer.[43] However, MRCP is not efficient at localizing a cholecystocholedochol fistula.[23]

**ERCP**

Despite its invasiveness, ERCP is considered a gold standard diagnostic tool for Mirizzi Syndrome with a mean sensitivity rate of 76.2%. [11,27] Indeed, Xie-qun et al[16] reported a 100% sensitivity rate for ERCP. This technique yields superior visualization of the extra-hepatic bile ducts, and can clearly show extrinsic compression by impacted gallstones in the CBD with resulting proximal biliary dilatation. Furthermore, ERCP can accurately determine the presence and location of fistula and biliary obstruction. Therapeutic decompression by papillotomy and stent or nasal bile drainage (NBD) can be achieved during ERCP.[16,20] Moreover, an endoscopic NBD tube placed during ERCP allows the outcome of surgery to be assessed through endoscopic NBD cholangiography, thus facilitating minimally-invasive laparoscopic surgery for Mirizzi Syndrome.[20] However, ERCP can also be associated with devastating complications and its application in patients suffering Mirizzi Syndrome should be considered with significant caution.[8]

**Other Modalities Of Diagnosis**

The combination of ≥2 diagnostic modalities has become common place in the management of Mirizzi Syndrome. However, this practice is not supported by strong evidence and there is currently no consensus among experts in terms of the added benefit of this practice. [23]

Other, less traditional modalities of diagnosis are also reported in the literature. For instance, percutaneous transhepatic cholangiography offers a reasonable option for diagnosis and the relief of obstructive symptoms preoperatively, especially when endoscopic treatment fails.[34,44] Furthermore, intraductal ultrasonography can expose defects in the ductal mucosa, suggesting the presence of a cholecystocholedochol fistula.[36,44,45] Endoscopic ultrasound (EUS) can also be performed prior to ERCP to further evaluate the bile ducts and pancreas and to determine the cause of biliary strictures.

For example, Rayapudi et al[34] reported one case of Mirizzi Syndrome Type I by EUS examination.

**Intraoperative Diagnosis**

A large number of patients are only diagnosed with Mirizzi Syndrome during surgery.[46] Surgery can reveal a range of signs associated with Mirizzi Syndrome, such as an edematous or atrophic gallbladder with distortion of Calot



triangle, an impacted gallstone in the infundibulum or the neck of the cystic duct, thick fibrosis around Calot triangle, and adhesions under the liver space. Cholecystobiliary fistula is strongly suspected if the extraction of an impacted stone is followed by the leakage of bile from the bile duct.[16] Further intraoperative cholangiography can then be used to ascertain the position and dimension of the fistula, detect stones in the duct, and verify the integrity of the bile duct wall, as well as retrieve residual stones in the postoperative setting. However, there is some concern that this technique is challenging to perform and carries a significant risk for secondary injury to the bile duct due to the distorted anatomy commonly encountered at Calot triangle.[8]

#### Treatment Of Mirizzi Syndrome

Surgical management is the mainstay treatment for Mirizzi Syndrome, although this is challenging for several reasons. First, there is a low index of suspicion for this condition among surgeons, largely owing to its rarity, as gallbladder surgery is often performed in patients with relatively shorter histories of illness, long before the onset of Mirizzi Syndrome.[27] Secondly, preoperative diagnosis is often missed, thus impacting upon the ability to treat this condition during surgery. Thirdly, distortion of the anatomy by dense adhesions due to longstanding inflammation and the advancement of cholecystobiliary or cholecysto-enteric fistula, increases the risk of bile duct injury or massive hemorrhage during dissection of Calot triangle.

Furthermore, inflammation can cause cutaneous fistula, secondary biliary cirrhosis, delayed onset biliary strictures, and even death. (Tables 2 and 3) present treatment choices according to the different subtypes of Mirizzi Syndrome found during our literature review.

#### Open Surgical Approach

Traditionally, laparotomy has been considered as the technique of choice for the management of Mirizzi Syndrome. This is largely due to its relative safety when compared with the laparoscopic technique which is associated with high conversion rates (31–100%) and an increased incidence of bile duct injury. However, laparotomy has the advantage of better visualization, haptic feedback, and gallbladder calculus removal before cholecystectomy despite its more invasive nature, high complication rate, and longer postoperative hospital stay.

Total cholecystectomy is feasible in cases of Mirizzi Syndrome Type I which are not associated with cholecystobiliary fistula. When severe inflammation impedes the safe dissection of Calot triangle, retrograde fundus-first cholecystectomy or partial (subtotal) cholecystectomy (PC or SC, respectively) can be applied.[16,22] Occasionally, it is necessary to visualize the CBD to manage other causes of obstructive jaundice. One earlier case reported intraoperative bile duct injury which was managed by Roux-en-Y hepaticojejunostomy (RYHJ).[26]

In some cases, T-tube insertion into the bile duct is necessary, not only to decompress the bile duct, but also to shape the duct in order to minimize the risk of bile leakage, especially when the quality of tissue repair is doubtful. This technique can also be used to dispose of retained stones during intervention radiology.

PC or SC leaves a cuff of gallbladder or cystic duct remaining that can be used to repair the fistula of CBD (choledochoplasty), a technique applicable in Mirizzi Syndrome type II and selected type III cases.[16,21–23,25,30] However, choledochol-enteric anastomosis is a preferred alternative to this method.

Some authors consider that it is safer to curve the fundus of the gallbladder and extract its contents before applying PC or SC.

This procedure has also been used in laparoscopic cholecystectomy.

#### Preoperative Biliary Decompression

In order to avoid postoperative complications, Le Roux et al[30] applied preoperative drainage with endoscopic stent, or a nasobiliary drain, placement by ERCP to avoid the insertion of T-tubes or abdominal drains. Preoperative biliary drainage facilitates the intraoperative identification of the main bile duct. For Type IV, there is consensus that the best surgical technique is cholecystectomy and RYHJ. However, some authors support the view that the presence of a fistula with a diameter wider than two-thirds of the CBD (Type III and Type IV) should warrant RYHJ.[16–18,22] The safest approach to manage Mirizzi Syndrome Type V is always laparotomy.

#### Laparoscopic, Endoscopic And Robot-assisted Techniques Laparoscopic Technique

The minimally-invasive laparoscopic approach has many advantages, including a shorter hospital stay and a reduced waste of resources. However, when applied to Mirizzi Syndrome, conversion rates are disappointingly high. Among the studies we reviewed, the conversion rate ranged from 11.1% to 80%. It is, therefore, reasonable for some experts to recommend limiting the laparoscopic approach to managing Type I only, as more severe inflammation and anatomical distortion would increase the risk of bile duct injury. In a series of 23 patients, attempts at LC for Mirizzi Syndrome were successful in only 1 patient (Type II).[17] Thereafter, the author preferred to use open surgery. Despite the risks and associated technical difficulties, some experts continue to recommend LC and laparoscopic subtotal cholecystectomy (LSC) for type II, and even type III. When performed, LSC is similar in detail to PC or SC in laparotomy. Kamalesh et al[24] performed LSC and bilioenteric anastomosis with T-tube placement for patients with type III. Rohatgi and Singh[47] described a step by step description of the laparoscopic procedure that emphasizes the classical section of the gallbladder fundus, identification of the infundibulum and cystic duct ab intra the gallbladder by taking out the impacted calculus, and further stated that these procedures could help to materialize the subtotal cholecystectomy. In such cases, intraoperative cholangiography is mandatory. Recently, a case report by Yeti ir et al[48] described a case of Mirizzi Syndrome Type V in which LSC was performed, along with resection of a cholecystocolic fistula and application of Tri-Staples.

#### Endoscopic Techniques

These methods play an important part in the management of Mirizzi Syndrome. Patients with Mirizzi Syndrome Types I, II, and III undergo ERCP preoperatively with sphincterotomy and NBD insertion, and then with LSC. NBD is used intraoperatively to decompress the bile duct, identify the CBD and to perform an intraoperative cholangiography. In some cases, T-tube insertion is avoided by NBD insertion. The successful use of this method for Type III was described by Li et al,[20] who performed LC combined with intraoperative choledochoscopy and Roux-en-Y reconstruction.

Sometimes it is necessary to use laser lithotripsy (LL), electrohydraulic lithotripsy (EHL), mechanical lithotripsy, or chemical dissolution of residual stone fragments. LL is the most commonly used method for this. Yeti ir et al[38] proposed single-operator cholangioscopy-guided LL and conventional cholangioscopy-guided LL, which have a 100% success rate for retrieving stones. However, it is absolutely critical for these methods that the surgeons involved are highly proficient in endoscopy.

#### Robot-assisted Techniques

Over recent years, a number of authors have emphasized the importance of robot-assisted techniques in the treatment of Mirizzi Syndrome.[19,31,49] Compared with laparoscopy,

robot-assisted systems can provide enhanced visualization with a three-dimensional camera, and surgeons can perform professional fine-tissue manipulation with endowrist instruments. Furthermore, to avoid partial cholecystectomy and its pertinent complications, the robot-assisted technique is safe and feasible for the takedown of cholecystocholedochal fistulas present in Mirizzi Syndrome, without partial cholecystectomy.[49,50] When combined with endoscopic techniques, the outcomes of these treatments can be even better.

**Other New Approaches**

Recently, Chuang et al[29] introduced laparoscopic trans-fistulous bile duct exploration, which features a combination of LSC and infundibulotomy, to perform EHL or LL for Type II, III, and IV. Others (Jones and Pawa[14] and Kim et al[36]) have described the application of single-operator peroral cholangioscopy. For post-cholecystectomy Mirizzi Syndrome type I, Donatelli et al[32] performed cystic duct balloon dilation at junction of the CBD and cystic duct stump, while Odemis et al[37] performed double cannulation followed by sphincterotomy and large balloon dilatation of papilla.

**CONCLUSIONS**

At present, Mirizzi Syndrome is managed in the clinic without well-developed, internationally-recognized clinical guidelines. Furthermore, advancement in diagnostic techniques has not made it easier for a confirmed diagnosis to be made before surgery, even though diagnostic rates have improved markedly. More often than not, laparotomy is chosen as the mode of treatment, as more experts have made attempts to popularize minimally-invasive treatment techniques. LSC is feasible for Type I, but can be selectively applied to Type II and even Type III. Endoscopy and robot-assisted surgery, with or without EHL or LL, currently stand as the best auxiliary methods. Nevertheless, procedures for the diagnosis or treatment of Mirizzi Syndrome, whether old or new, are limited by small sample sizes and there is a clear need to design and implement further studies which investigate a larger number of cases, and therefore provide evidence-based data with which to create a standard of management for Mirizzi Syndrome.

**FOOTNOTES**

Abbreviations: ALT = alanine aminotransferase, AST = aspartate transaminase, CBD = common bile duct, CHD = common hepatic duct, CT = computed tomography, EHL = electrohydraulic lithotripsy, ERCP = endoscopic retrograde cholangiopancreatography, EUS = endoscopic ultrasound, LC = laparoscopic cholecystectomy, LL = laser lithotripsy, LSC = laparoscopic subtotal cholecystectomy, MRCP = magnetic resonance cholangiopancreatography, MS = Mirizzi Syndrome, NBD = nasal bile drainage, PC or SC = partial (subtotal) cholecystectomy, RYHJ = Roux-en-Y hepaticojejunostomy, US = ultrasound.

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