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Clinical Outcomes and Treatment Strategy of Mirizzi's Syndrome Treated with Surgery: A Retrospective Analysis

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1. Abstract

1.1. Objective: To explore the surgical treatment strategy for Mirizzi's syndrome (MS) by analysing its clinical characteristics and treatment outcomes.

1.2. Methods: This retrospective study analysed the clinical data of 130 patients with MS who underwent surgery at our hospital from April 2013 to April 2020. Their diagnosis and treatment were summarised based on our single-centre management experience.

1.3. Results: The study population comprised 130 patients with MS, with an approximately balanced sex ratio and a median age of 58.5 years. The duration of the disease ranged from 4 h to 40 years, and only three patients were asymptomatic, while the remaining patients presented with symptoms such as abdominal pain, jaundice, or fever. The laboratory results revealed increased levels of direct bilirubin, alkaline phosphatase, and gamma-glutamyltransferase. The preoperative diagnostic rate was 82.3%, including 30.8% of cases diagnosed through ultrasound, 82.6% through magnetic resonance cholangiopancreatography, and 92.5% through endoscopic retrograde cholangiopancreatography. The intraoperative diagnostic rate was 17.7%. All patients underwent surgical treatment, with 74 cases of laparoscopic surgery, 43 cases of laparotomy, and 13 cases of laparoscopic surgery converted to laparotomy. The postoperative complication rate was 17.7%, mostly due to biliary leakage, abdominal infection and recurrence of stones. There was no significant difference in the incidence of complications between laparoscopic and open surgery.

1.4. Conclusions: MS diagnosis typically requires a combination of two or more examinations, as a single test might not help establish a diagnosis. Clear preoperative diagnosis can significantly reduce postoperative complications. The primary treatment for MS is surgery, with the choice of modality determined by MS classification and treatment centre proficiency. Our study demonstrated that laparoscopic surgery was a safe and feasible option for MS treatment.

2. Introduction

Mirizzi's syndrome (MS) is a rare condition caused by stones from the bile duct or gallbladder neck that compress the common hepatic duct and form a cholecystocholedochal fistula, resulting in obstructive jaundice, fever, and right upper abdominal pain. Due to its non-specific nature, preoperative diagnosis is challenging [1], and MS is a frequent cause of bile duct injury, making early diagnosis critical. However, due to the low incidence and unusual clinical manifestations, a definitive diagnosis usually requires two or more imaging tests. Surgery is the primary treatment option for

MS, with laparotomy previously preferred over laparoscopic surgery [2]. Nevertheless, advances in laparoscopic techniques and equipment have made laparoscopic surgery a viable treatment option for MS in more experienced hepatobiliary centres. However, the choice of surgical approach varies based on MS classification and the degree of inflammation and erosion of adjacent structures. This study retrospectively analysed clinical data from 130 patients with MS who underwent surgical treatment at our hospital between April 2013 to April 2020 to summarise our experience in treating MS.

3. Materials and Methods

3.1. General Information

We conducted a retrospective analysis of 130 patients with MS who were surgically treated at our hospital between April 2013 and April 2020. The study analysed the patient's demographic data, clinical manifestations, laboratory and imaging findings, diagnosis and classification, surgical modalities, and postoperative outcomes. The classification of patients with MS followed the criteria proposed by Csendes et al., [3], which classified patients into types I to IV based on the location and extent of stones and the resulting damage to the common hepatic duct. Those with type I have stones embedded in the neck of the gallbladder or the cystic duct, compressing the common hepatic duct and causing partial stenosis of the common hepatic duct; those with type II had stones embedded in the common hepatic duct, resulting in the formation of a cholecystocholedochal fistula; however, the fistula was less than one-third of the circumference of the common bile duct; those with type III had a fistula measuring one-third to two-third of the circumference of the common bile duct; those with type IV had a cholecystocholedochal fistula that destroyed the common bile duct; those with type V were classified as type Va (without intestinal obstruction) and type Vb (with intestinal obstruction) based on the method proposed by Beltren et al.[4]. This study was approved by the hospital's ethics committee, and Written patients informed consent was waived by the ethics committee.

3.2. Surgical Method

Surgery was the definitive treatment for MS, and intraoperative confirmation of the diagnosis was obtained. laparoscopic surgery: Total cholecystectomy or subtotal cholecystectomy was used to treat type I MS. If the bile duct was significantly dilated, further exploration could be performed through the cystic duct or by opening the anterior wall of the common bile duct. Subtotal cholecystectomy involved the removal of a large portion of the gallbladder, removal of stones in the gallbladder or the cystic duct, and ligation of the residual gallbladder with sutures or a ligature. For type II MS, the gallbladder was opened, the stones were removed, and the choledochoscope was accessed through the gallbladder fistula. If the fistula was small and the choledochoscope could not be accessed, a small incision was made on the anterior wall of the common bile duct and the choledochoscope was accessed to explore the bile duct. Stones were removed together, and the T-tube was inserted into the bile duct via the reverse insertion method, with the short arm of the T-tube crossing the defect. The treatment for type III and IV MS was similar to that of type II MS. We preserved as much tissue as possible from the residual gallbladder and ampulla, and after the bile duct was explored; choledochoplasty was performed using the residual gallbladder wall, following which the T-tube was fixed (Figure 1A-D). If the residual gallbladder wall tissue was inadequate, fragile, and severely oedematous, it was difficult to use the residual wall as the bile duct wall, for which a biliary-intestinal anastomosis was performed. For type V MS, cholecystectomy was performed, and gastrointestinal fistula was repaired or protective gastrostomy was performed.

Open surgery: The patient was supine, and the right oblique incision under the costal margin or the right transrectus abdominalis incision was made to enter the abdomen layer by layer and explore the abdominal cavity. The gallbladder was resected retrograde first, and the rest of the procedure was the same as that of the laparoscopic surgery.

Laparoscopic conversion to open surgery: When there were intraoperative anatomical difficulties or bleeding, the procedure was converted to open surgery. Generally, the right oblique incision under the costal margin or the right transrectus abdominalis incision was made to enter the abdomen layer by layer. The rest of the procedure was the same as laparoscopic surgery.

Figure 1: Laparoscopic surgical procedure in patients with type III MS
A. Subtotal cholecystectomy was performed and the stone was removed through the fistula opening

B. The cholangioscope explored the intra- and extrahepatic bile ducts through the fistula opening

C. A incision in the anterior wall of the bile duct was performed below the fistula and a T-tube was inserted into the bile duct with its short arm crossing the defect

D. The residual ampulla tissue of gallbladder and bile duct wall were used to repair and shape of the bile duct

3.3. Follow-up

Patients were followed up by telephone, including recurrence of bile duct stones, bile duct stenosis, and treatment modalities, up to 30 September 2023.

3.4. Statistical Analysis

Statistical analysis was performed using SPSS 22.0 software. Normally distributed measures are expressed as the mean ± standard deviation, and independent samples t-test was used for between–group comparisons. Non-normally distributed measures are expressed as the median (Q1, Q3), and the rank sum test was used for between-group comparisons. Enumeration data are expressed as frequencies (%), and the chi-square test or Fisher's exact test was used for between-group comparisons. Statistical significance was set at $p < 0.05$.

4. Results

Of the 130 patients with MS patients, 61 were males and 69 were female, with ages ranging from 18 to 86 years and a median age of 58.5 years. The duration of the disease ranged from 4 h to 40 years, with 23 cases having a disease duration of over 10 years. Except for three asymptomatic, all patients experienced abdominal pain, where 44 cases had abdominal pain, two cases had jaundice, and one case had fever as the only symptom. The remaining patients had two or more symptoms, of which 51 cases had abdominal pain with jaundice, five cases had abdominal pain with fever, two cases had jaundice with fever, and 22 cases had manifestations of acute cholangitis, typical of the Charcot's triad. Liver function was normal in 18 of the 130 patients with MS, while the rest had varying degrees of liver damage. Table 1 summarises the patients' demographic data, clinical characteristics, and laboratory data.

Of the 130 patients with MS, 107 cases received a preoperative diagnosis while 23 were diagnosed intraoperatively. Ultrasound examinations were performed on all patients, with only 40 cases accurately diagnosed, resulting in a 30.8% accuracy rate. Three additional cases suggested the possibility of biliary pneumatosis and an internal fistula between the gallbladder and intestine. Magnetic resonance cholangiopancreatography (MRCP) examinations were performed on 86 cases, and 71 cases were accurately diagnosed, with an accuracy rate of 82.6%. Endoscopic retrograde cholangiopancreatography (ERCP) examinations and treatment were performed on 53 cases, resulting in 49 accurate diagnoses and an accuracy rate of 92.5%. No statistical difference was observed between the diagnostic rates of MRCP and ERCP; however, the diagnostic rates of MRCP and ERCP were significantly higher than those of B-mode ultrasound (BUS), which were statistically different (Table 2). Preoperative MS diagnosis and classification relied heavily on two or more imaging examinations, particularly ERCP, as BUS was insufficient to determine the classification. In our study, a total of 53 cases of ERCP were examined and treated before operation, including 49 cases of ERCP+EST+ENBD and 4 cases of ERCP+EST+ERBD. Of the 107 patients with a clear preoperative MS diagnosis, BUS suggested MS in eight cases, ERCP in 18 cases, MRCP in 40 cases, BUS + ERCP in five cases, BUS + MRCP in 17 cases, BUS + MRCP + ERCP in 10 cases, and MRCP + ERCP in nine cases. Among them, 48 cases were classified as type I, nine as type II, 19 cases as type III, 28 cases as type IV, and three as type V (Table 3).

All patients received surgical treatment eventually, and the diagnosis of MS was further clarified intraoperatively. In 23 cases, the diagnosis was made intraoperatively as it was unclear before surgery. The types of MS diagnosed intraoperatively were 11 cases of

type I, four cases of type II, two cases of type III, four cases of type IV, and two cases of type V. Of all patients with MS, There were 74 cases underwent laparoscopic surgery, 43 cases underwent laparotomy, and 13 cases of laparoscopic surgery were converted to laparotomy. Among the 32 cases of type IV MS, 21 of them could be completed by laparoscopic surgery. Of the five cases of type V MS, only one case successfully underwent laparoscopic surgery, while two of the remaining four cases underwent laparoscopic surgery, which were converted to laparotomy. In all patients, o biliary-intestinal anastomosis was only performed on one case of type IV, and the rest underwent choledochoplasty through the residual gallbladder wall to avoid biliary tract reconstruction. The surgical details are presented in (Table 4).

Postoperative complications occurred in 23 cases, resulting in an incidence rate of 17.7%. No perioperative deaths occurred. Early complications included three cases of biliary leakage, one case of bleeding from the stump of the cystic artery, which was resolved by digital subtraction angiography embolisation, two cases of incisional fat liquefaction, one case of incisional infection, one case of duodenal fistula in a type V patient, one case of type I with a cystic duct stone migrating into the common bile duct that was treated by ERCP lithotripsy, and three cases of abdominal infection, all of which were recovered following treatment by abdominal puncture and drainage. Long-term complications included bile duct stenosis in one patient, which was treated by ERCP+ERBD, and recurrent bile duct stones in 10 patients, with the recurrence rate of 7.7%, which were all treated by ERCP (Table 5). There was no significant difference in the incidence of complications between laparoscopic surgery (12.3%) and open surgery (5.4%).

Table 1: General data statistics, N=130

Gender	
Male	61(46.9%)
Female	69(53.1%)
Age, median (range)	58.5(18-86)
Course of the disease	
<10 year	107(82.3%)
≥10 year	23(17.7%)
Clinical presentation	
No	3(2.3%)
Pain	44(33.8%)
Jaundice	2(1.5%)
Fever	1(0.8%)
Pain and Jaundice	51(39.2%)
Pain and Fever	5(3.8%)
Jaundice and Fever	2(1.5%)
Pain, Jaundice and Fever	22(16.9%)
Labratory data, M(P_{25},P_{75})	
TBIL[umol/L,M(P_{25},P_{75})]	55.3(21.1,128.1)
DBIL[umol/L,M(P_{25},P_{75})]	26.0(7.5,96.7)
ALP[U/L,M((P_{25},P_{75})]	149.0(81.0,279.0)
GGT[U/L,M((P_{25},P_{75}))]	253.0(46.8,672.3)
ALT[U/L,M((P_{25},P_{75}))]	130.5(30.8,321.0)

Table 2: Imaging examination, N=130

Imaging examination	Examine	Diagonose	Rate of diagonose (%)
BUS	130	40	30.8%[a]
MRCP	86	71	82.6%[b]
ERCP	53	49	92.5%[c]

[a] Compared with MRCP group, P<0.05; [b]Compared with ERCP group, P>0.05; [c] Compared with BUS group, P<0.05

Table 3: Diagonose data, N=130

Diagonose data	Total (%)	MSI	MSII	MSIII	MSIV	MSV
Preoperative diagonose	107(82.3%)	48	9	19	28	3
Operative diagonose	23(17.7%)	11	4	2	4	2

Table 4: Operative procedures, N=130

Operative procedures	Total(%) N=130	MSI N=59	MS II N=13	MSIII N=21	MSIV N=32	MS V N=5
Open cholecystectomy	7(5.4%)	6	1	0	0	0
Laparoscopic cholecystectomy	34(26.2%)	33	0	0	1	0
Open cholecystectomy+ CBD exploration	31(23.8%)	11	6	7	7	0
Laparoscopic cholecystectomy+CBD exploration	31(23.8%)	2	2	7	20	0
Open cholecystectomy +transcystic	2(1.5%)	1	0	0	1	0
Laparoscopic cholecystectomy+transcystic	8(6.2%)	3	1	4	0	0
Bilioenteric anastomosis	1(0.8%)	0	0	0	1	0
Cholecystectomy+repair of digestive tract fistula	3(2.3%)	0	0	0	0	3
Conversion	13(10%)	3	3	3	2	2

Table 5: Postoperative morbidity, N=23

Morbidity	Total 23(17.7%)	Laparoscopic operation 16[a](12.3%)	Open operation 7(5.4%)
Bile leakage	3(2.3%)	2(1.5%)	1(0.8%)
Bleeding	1(0.8%)	1(0.8%)	0(0)
Wound liquefaction	2(1.5%)	1(0.8%)	1(0.8%)
Wound infection	1(0.8%)	0(0)	1(0.8%)
Duodenal fistula	1(0.8%)	1(0.8%)	0(0)
Retained stones	1(0.8%)	1(0.8%)	0(0)
Abdominal infection	3(2.3%)	3(2.3%)	0(0)
Recurrence of stones	10(7.7%)	6(4.6%)	4(3.1%)
Biliary stenosis	1(0.8%)	1(0.8%)	0(0)

[a]Compared with open operation, P>0.05

5. Discussion

The incidence of MS is relatively low, occurring in only 0.1% of patients with gallstones and 0.7% to 25% of patients with cholecystectomy. While the prevalence might be higher in the elderly population, it is not associated with any specific ethnic group, and there is no significant difference in the occurrence between male and female patients with gallstones [5]. In this study, we analysed a larger sample size at our centre and summarised our experience and lessons learned in treating MS, as our understanding of the condition has improved and our techniques have become more refined, resulting in satisfactory outcomes.

MS can have a long duration, lasting over 10 years in 17.7% of cases, or can present acutely, making it challenging to diagnose based solely on disease duration. The clinical manifestations of MS are non-specific, with only 2.3% of 130 patients showing no symptoms, and most experiencing abdominal pain (33.8%) commonly in the right upper abdomen or subxiphoid. Very few patients had only one symptom of jaundice or fever. Patients with MS often present with two or more symptoms, with 16.9% of patients exhibiting Charcot's triad. It is challenging to diagnose MS based solely on clinical symptoms, as it can present with symptoms similar to acute cholecystitis, acute pancreatitis, acute cholangitis, or cholangiocarcinoma, requiring differentiation from these diseases.

Kwon et al., [6] found that serum bilirubin levels were normal in approximately 20-40% of patients and elevated in 33% of patients with visible jaundice. However, Gonzalez-Urquijo et al., [7] reported different results, with 18% of their 22 patients with MS having normal serum bilirubin levels and 59% having elevated levels. In our study of 130 patients, 53 (41%) had normal serum bilirubin levels, which is consistent with Kwon et al.'s findings. We observed elevated serum bilirubin levels in 77 (59%) patients, which is similar to Gonzalez-Urquijo et al.'s findings.

The reported diagnostic rates of MS vary widely among imaging modalities. Ultrasound has a diagnostic rate ranging from 0% to

50%, while computed tomography (CT) has a diagnostic rate of 25-31%, MRCP has a rate of 50-63%, and ERCP has a rate of 58-76.2% [8,9]. Combining multiple modalities can improve the preoperative diagnostic rate to 29.6-85.9% [8]. Although ultrasound is the most common modality for diagnosing gallstones, its sensitivity is limited. CT is not sensitive to MS but can differentiate it from malignancy. MRCP has better diagnostic accuracy than CT and has the added advantage of avoiding complications associated with ERCP [10]. ERCP remains the gold standard for diagnosis [12], with a diagnostic accuracy of approximately 75%, and sensitivity ranging from 50% to 100% [11]. The prevalence of MS in patients undergoing ERCP is estimated to be 1.07% [10]. In our study, we performed preoperative ultrasound on all patients, resulting in a diagnostic accuracy of 30.8%. MRCP detected 86 cases with a diagnostic accuracy of 82.6%, while ERCP examined and treated 53 cases with a diagnostic accuracy of 92.5%. The diagnostic rates of MRCP and ERCP were significantly higher than those of BUS and showed statistical significance. However, there was no significant difference between the diagnostic rates of MRCP and ERCP. Therefore, either MRCP or ERCP could be the preferred choice for patients with abnormal BUS or laboratory findings that require further investigation. Our study achieved an overall preoperative diagnosis of 82.3% for patients with MS, which is consistent with the literature and is attributable to the increased use of MRCP and ERCP examinations. The preoperative diagnosis of MS is considered critical to the success of treatment [13] and avoiding complications [14].

In patients with jaundice or BUS indicating bile duct dilatation, MRCP is routinely performed as a standard procedure to prevent intraoperative bile duct damage and confirm the diagnosis. However, in patients without jaundice and BUS indicating gallbladder stones or gallbladder neck stones, intraoperative exploration is relied upon to confirm the diagnosis. While BUS can aid in the diagnosis of MS, it does not provide definite classification, which requires additional diagnostic tools such as MRCP. For older patients with chronic inflammation and multiple underlying diseases, due to the high risk of surgery, it is not suitable to undergo surgical treatment. They can choose to undergo ERCP for stone removal and biliary stent placement. For patients with acute cholangitis or severe biliary infection, it is not the time for surgical treatment. ERCP should be chosen to place a nasobiliary tube for drainage, first to relieve biliary obstruction and further confirm the MS type. Surgery can be performed after infection control. For patients diagnosed with MS before surgery, the preoperative application of ERCP plays a critical therapeutic role in preventing intraoperative biliary tract injury. Additionally, ERCP offers therapeutic benefits in terms of postoperative residual bile duct stones and bile duct stenosis. ERCP is a critical component of the comprehensive treatment plan for MS, as stated by Yeh et al [15].

The most evident characteristic of type V MS is bile duct pneumobilia. An internal fistula between the gallbladder and the intestine results in intestinal hypertension, with ectopia of microbiota, leading to biliary pneumatosis. Patients without a history of digestive tract reconstruction should be cautious about the possibility of type V MS if they exhibit biliary pneumatosis. In our study, we identified five cases of type V MS, of which three cases showed ultrasound results suggestive of bile duct pneumatosis and a potential internal fistula between the gallbladder and the intestine. However, the diagnosis of type V MS cannot be confirmed by ultrasound alone and requires a combination of MRCP examination or even intraoperatively examination for a definitive diagnosis. In our study, two cases were diagnosed with ultrasound + MRCP, one case with ultrasound + MRCP + ERCP, and two cases with intraoperative diagnosis. Reportedly, Type V MS is most commonly Type Va, involving adjacent organs such as the stomach, duodenum, and colon[4]. The type V MS we found were all Type Va gallbladder gastric fistulas and gallbladder duodenal fistulas, consistent with the literature. Due to the small number of Type Va cases in our data, we have not yet found the gallbladder colon fistulas reported by Mauricio et al[16].

In our study, type I MS was the most prevalent, accounting for 45.4% of cases, while types II, III, and IV MS were less common, accounting for 10%, 16.2%, and 24.6%, respectively. Type V was the rarest, accounting for only 3.8%. According to previous reports [17], type I MS is typically treated with total cholecystectomy or subtotal cholecystectomy, while type II requires major cholecystectomy with bile duct reconstruction, and types III and IV require biliary-intestinal anastomosis. Our findings suggest that type I MS usually does not involve a cholecystocholedochal fistula. Thus, a gap between the cystic duct and the common hepatic duct persists. Total cholecystectomy could be successfully performed, and subtotal cholecystectomy was rarely used. If the bile duct was dilated, bile duct exploration was performed together without choledochoplasty. In our study, there were 59 cases of type I MS, and 39 cases were performed with simple cholecystectomy. As some surgeons lacked experience, they did not consider this condition as MS, particularly while performing a laparotomy, wherein the field of view is not as wide as that in laparoscopy. Therefore, the actual incidence of type I MS was higher. The most effective strategy for type II MS is to explore the bile duct through a cholecystic fistula and then drain it using a T-tube through the fistula [18]. Typically, biliary reconstruction is not necessary for most cases of type II MS. Kamalesh et al., [19] successfully completed 70% of type II and III MS procedures using laparoscopy. They suggested that surgeons perform a subtotal cholecystectomy while preserving the remnants of Hartman's pouch and use it to construct choledochoplasty. Stone removal is the primary objective in treating patients with MS, and laparoscopic subtotal cholecystectomy can be a useful approach to avoid bile duct injury [20]. We believe

that subtotal cholecystectomy is a safe and effective option. For patients with type III and IV MS with more extensive disruption of bile duct continuity, the conventional treatment principle is biliary-intestinal anastomosis [21-23]. In our opinion, biliary-intestinal anastomosis is associated with an increased risk of postoperative biliary epithelial infection and reflux cholangitis due to the disruption of Oddi sphincter function, which can negatively affect the patient's quality of life. Therefore, we typically opt for cholecystectomy, bile duct exploration, T-tube drainage, bile duct repair, and choledochoplasty. If the residual gallbladder wall is severely oedematous, defective, and fragile, biliary-intestinal anastomosis is considered. Among the 130 patients in our study, only one patient with type IV MS underwent biliary-intestinal anastomosis. The incidence of type V MS was low, accounting for only five out of 130 (3.8%) patients, all of whom were classified as type Va according to the classification criteria by Beltren et al. We managed these cases by repairing the gastrointestinal fistula, with protective gastrostomy if necessary.

In our study, Postoperative complications occurred in 23 patients (17.7%), and no deaths occurred during perioperative period. The incidence of complications was lower than the 22.7% reported by Gonzalez-Urquijo et al [7]. The occurrence of complications in patients with MS was associated with preoperative diagnosis, choice of surgical approach, and the surgeon's technical skills. Ji et al., [24] reported a higher risk of complications in patients with MS due to the large proportion of intraoperative diagnoses made. Conversely, in our study, the preoperative diagnostic rate was 82.3%, which played a crucial role in reducing postoperative complications. In addition, there was no statistical significance in the incidence of complications between laparoscopic surgery and open surgery, which proved that laparoscopic surgery was safe and feasible.

In conclusion, MS is a rare disease that can be easily overlooked due to its non-specific clinical manifestations and laboratory findings. Patients with preoperative jaundice or ultrasound findings suggestive of bile duct dilatation should undergo further MRCP or ERCP to improve the preoperative diagnosis of MS and avoid iatrogenic injury to the biliary tract. The treatment modality for MS depends on its severity, as defined by the Csendes classification. Treatment plans should be individualised for each patient, with surgery being the ultimate treatment. However, there are no established clinical guidelines for treating each type of MS. The treatment for types I and II is relatively straightforward, whereas the treatment of types III and IV is more controversial. The choice of treatment modality should be based on the centre's technical expertise, and laparoscopic surgery is safe and feasible, and the combination with ERCP surgery is a key part of the treatment strategy.

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