The Relationship of Mirizzi Syndrome and Cholecystoenteric Fistula: Validation of a Modified Classification

Marcelo A. Beltran · Attila Csendes · Karina S. Cruces

Abstract

Background Mirizzi syndrome and cholecystoenteric fistula with or without gallstone ileus are late complications of gallstone disease. We previously suggested that the natural history of Mirizzi syndrome may not end with just a cholecystobiliary fistula and that the continuous inflammation in the triangle of Calot area may result in a complex fistula involving the biliary tract and the adjacent viscera. The purpose of this study was to establish the relationship of Mirizzi syndrome with cholecystoenteric fistulas.

Methods We retrospectively reviewed the records of all patients older than aged 18 years submitted to emergency or elective cholecystectomy from 1995 to 2006. Of 5,673 cholecystectomies performed during that period, we found 327 (5.7%) patients with Mirizzi syndrome and 105 (1.8%) patients with cholecystoenteric fistula. Ninety-four (89.5%) patients with cholecystoenteric fistula also had an associated Mirizzi syndrome.

Results Cholecystoenteric fistula was associated with Mirizzi syndrome ($p < 0.0001$), increased age was associated with Mirizzi syndrome and cholecystoenteric fistula ($p < 0.0001$), and female gender was associated with Mirizzi syndrome ($p < 0.0001$).

Conclusion When during surgery for gallstone disease a cholecystoenteric fistula is encountered, the possibility of an associated Mirizzi syndrome must be considered. The findings of this study confirm the association of Mirizzi syndrome with cholecystoenteric fistula.

M. A. Beltran · K. S. Cruces
Department of Surgery, Hospital De Ovalle, Ovalle, Chile

M. A. Beltran (✉)
Manuel Antonio Caro 2629, San Joaquin, P.O. Box 912,
La Serena, Región De Coquimbo, Chile
e-mail: beltran_01@yahoo.com

A. Csendes
Department of Surgery, Hospital Clínico De La Universidad
De Chile, Santiago De Chile, Chile

Introduction

Mirizzi syndrome and cholecystoenteric fistula with or without gallstone ileus are rare and late complications of gallstone disease [1, 2]. In most parts of the world, the widespread use of ultrasonography has led to early diagnosis and treatment for those with gallstone disease; however, some remote rural areas still have a higher prevalence of these uncommon complications due to difficult communications and limited access to basic technological resources, such as abdominal ultrasonography [2, 3]. The physiopathology of Mirizzi syndrome has been described by McSherry et al. [4] and Csendes et al. [5], establishing the sequence of events from the impaction of a gallstone to the erosion through the gallbladder and common bile duct wall forming a cholecystobiliary fistula. The same physiopathological process explains other biliary fistulas, such as cholecystoduodenal, cholecystogastric, and cholecystocolonic fistulas [2]. We previously suggested that the natural history of Mirizzi syndrome may not end with just a cholecystobiliary fistula and that the continuous inflammation in the triangle of Calot area may result in a complex fistula involving not only the biliary tract but also the adjacent viscera [2]. Based on this suggestion, Csendes et al. recently added a new type to his classification of Mirizzi syndrome [6]; this new classification includes a cholecystoenteric fistula complicating the other types (Table 1). We noticed in our institutional practice that many of our patients operated on for complicated gallstone

Table 1 New Mirizzi syndrome classification [6] (2007)

Type	Description
I	Extrinsic compression of the common bile duct by an impacted gallstone
II	Cholecystobiliary fistula secondary to an eroded gallstone involving one third of the circumference of the common bile duct
III	Cholecystobiliary fistula involving two thirds of the circumference of the common bile duct
IV	Cholecystobiliary fistula comprising the whole circumference of the common bile duct
V	Any type plus a cholecystoenteric fistula
Va	Without gallstone ileus
Vb	With gallstone ileus

disease had Mirizzi syndrome and also noticed that most cholecystoenteric fistulas were associated with Mirizzi syndrome, whereas few cholecystoenteric fistulas were not. The purpose of this study was to establish the relationship of Mirizzi syndrome with cholecystoenteric fistulas.

Patients and methods

Institutional setting

The institution were this study was performed is a community 250-bed hospital located in the city of Ovalle in the Chilean northern highlands. This hospital serves the 90,000 inhabitants of the city of Ovalle and 50,000 more people distributed in small isolated rural communities in an area comprising 17,000 km^2. For this reason, access to health resources, such as the hospital or small rural medical centers, is difficult for most of these people. Frequently they present with acute and chronic complications of gallbladder disease, and as a consequence in our institutional practice we operate on many patients with severe complications of gallstone disease, such as Mirizzi syndrome, cholecystoenteric fistula, and gallstone ileus [2].

Design of the study

This was an observational study; we retrospectively reviewed the records of all patients older than aged 18 years submitted to emergency or elective cholecystectomy from 1995 to 2002. From 2003 to 2006, we acquired data in a prospective database. A total of 5,673 cholecystectomies were performed during the 13-year period; among them we found 327 (5.7%) patients with Mirizzi syndrome and 105 (1.8%) patients with cholecystoenteric fistula. Ninety-four (89.5%) patients with cholecystoenteric fistula also had an associated Mirizzi syndrome and only 11 (10.5%) were not associated with Mirizzi syndrome. Consequently we studied 338 patients with Mirizzi syndrome and or cholecystoenteric fistula. The following variables were analyzed: age, sex, years of evolution of gallstone disease (from the onset of symptoms to surgery), the presence and type of Mirizzi syndrome according to Csendes et al. [5], the presence of cholecystoenteric fistula, number of fistulas and involved organs, type of surgical intervention, intraoperative and postoperative complications, mortality, and histopathology. We excluded all patients operated on for gallbladder cancer or other biliary tract carcinoma found incidentally during surgery or diagnosed in the preoperative study.

Statistics

Variables were reported as mean and standard deviation or as percentages. The correlation between Mirizzi syndrome and cholecystoenteric fistula was assessed with the Pearson correlation test with a significant value established at $p < 0.01$ (two-tailed). Other analyzed variables were the correlation between Mirizzi syndrome, sex, and age, and between cholecystoenteric fistula sex and age. The database was processed with the statistical software SPSS 11.0.

Results

Most patients were women with a mean age of 60 ± 12.4 years for patients with Mirizzi syndrome and associated cholecystoenteric fistula. Progression of gallstone disease from the first symptoms to surgery was prolonged in all patients with a mean period of 31.4 ± 15.2 years in patients with Mirizzi syndrome and cholecystoenteric fistula. Most patients were submitted to elective surgery; however, an important percentage of patients with Mirizzi syndrome and or cholecystoenteric fistula underwent emergency surgery for acute cholecystitis or gallstone ileus (Table 2). According to the Pearson bivariate correlation

Table 2 Demographics, years of gallstone disease, and indication for surgery

	Total ($n = 338$) (100%)	Mirizzi ($n = 327$) (96.5%)	Fistula ($n = 11$) (3.5%)
Men	109 (32%)	107 (32.7%)	2 (18%)
Women	229 (68%)	220 (67.3%)	9 (82%)
Age (mean ± SD)	59 ± 16.8	60 ± 12.4	58 ± 16.5
Gallstone disease (yr) (mean ± SD)	29.6 ± 15.6	31.4 ± 15.2	29.2 ± 15.7
Elective surgery	200 (59%)	193 (59%)	7 (64%)
Emergency surgery	138 (41%)	134 (41%)	4 (36%)

SD standard deviation

Table 3 Type of Mirizzi syndrome according to Csendes et al. [5] (1989)

Mirizzi	($n = 327$) (100%)
I	170 (52)
II	76 (23.2)
III	61 (18.6)
IV	20 (6.2)

test, we found the following associations: cholecystoenteric fistula was associated with Mirizzi syndrome ($p < 0.0001$), increased age was associated with Mirizzi syndrome and with cholecystoenteric fistula ($p < 0.0001$), and female gender was associated with Mirizzi syndrome ($p < 0.0001$) but not with cholecystoenteric fistula ($p = 0.759$). When we classified the Mirizzi's syndrome according to the classification described by Csendes et al. [5] in 1989, we observed that most patients had a Mirizzi type I (52%) and as expected the number of patients with other types of Mirizzi decreased, whereas the type was higher (Table 3).

Of 170 patients with Mirizzi I, 2.3% had associated a cholecystoenteric fistula, and 35.5% with Mirizzi II, 84.6% with Mirizzi III, and 60% with Mirizzi IV also had an associated cholecystoenteric fistula. Most patients with cholecystoenteric fistula associated with Mirizzi syndrome (84%) had types II and III ($p < 0.002$). In 15 patients, a double fistula was identified (Table 4). When we classified the Mirizzi's syndrome according to the new classification described by Csendes et al. [6], we observed that Mirizzi type I was still the most frequent type (Fig. 1), the other types were less frequent (Figs. 2–4) because most of these types were associated with cholecystoenteric fistulas, consequently they currently form part of Mirizzi type V (Fig. 5). Most of these patients presented without gallstone ileus (Type Va, 82 patients, 25%), and 12 patients had an associated gallstone ileus (Type Vb, 12 patients, 3.6%).

In most patients with Mirizzi I (92%) the surgical intervention consisted in cholecystectomy or cholecystectomy and intraoperative cholangiography (IOC). In four cases, a cholecystoenteric fistula was found and repaired with simple suture. Patients with Mirizzi II, III, or IV had a wide variety of surgical procedures performed. Frequent procedures in patients with Mirizzi II were partial cholecystectomy with suture of the remnant gallbladder and IOC (72.4%), and choledocostomy with repair of the cholecystoenteric fistula when present. Patients with Mirizzi III underwent more complex surgery, such as choledocoduodenostomy or Roux en Y hepaticojejunostomy, and in one

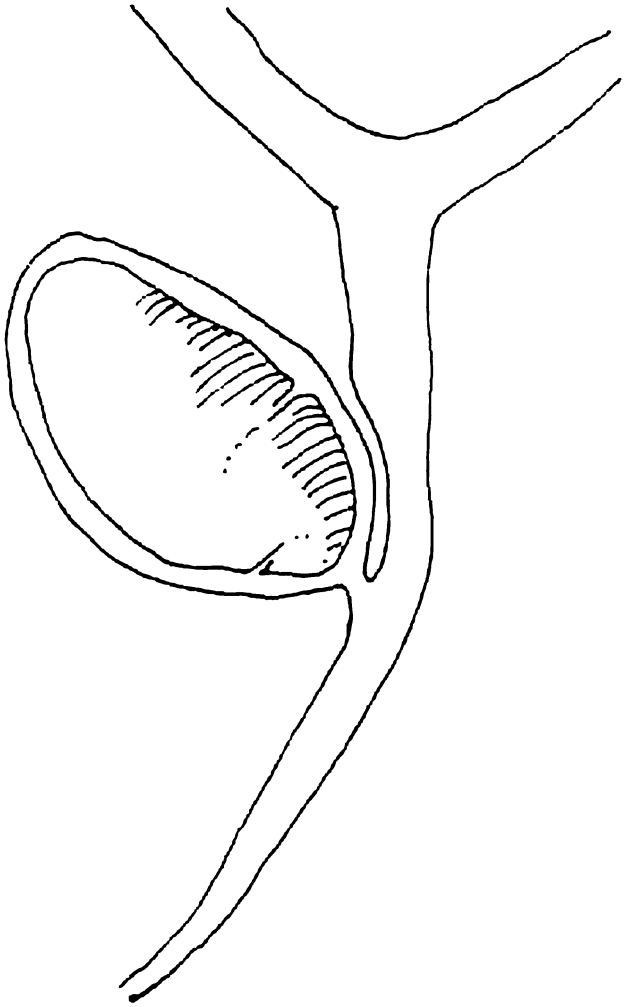

Fig. 1 Mirizzi syndrome type I. The extrinsic compression of the common bile duct by an impacted gallstone was present in 166 patients (51%)

Table 4 Organ involved in cholecystoenteric fistula associated to Mirizzi syndrome

	Mirizzi I	Mirizzi II	Mirizzi III	Mirizzi IV	Total ($n = 109$)[a] (100%)
Stomach	–	9	15	11	35 (32)
Duodenum	3	13	21	7	44 (40)
Colon	1	5	15	9	30 (28)
Total (n = 94)[b] (100%)	4 (4)	27 (29)	51 (54)	(13)	

[a] Includes 15 double fistulas

[b] Patients with Mirizzi syndrome and cholecystoenteric fistulas

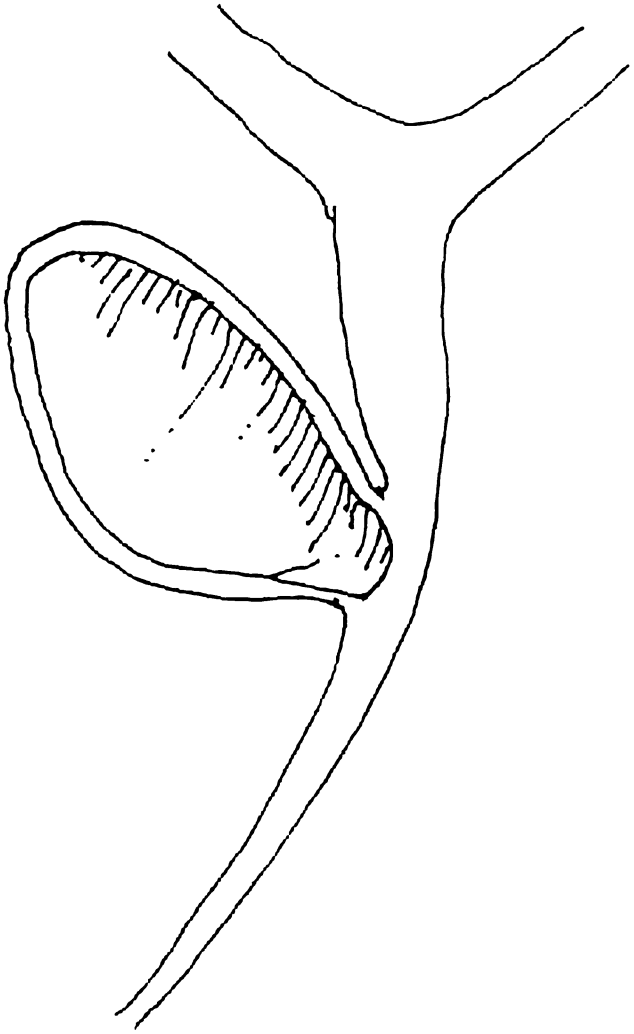

Fig. 2 Mirizzi syndrome type II. A cholecystobiliary fistula secondary to an eroded gallstone involving one-third of the circumference of the common bile duct was present in 49 patients (15%)

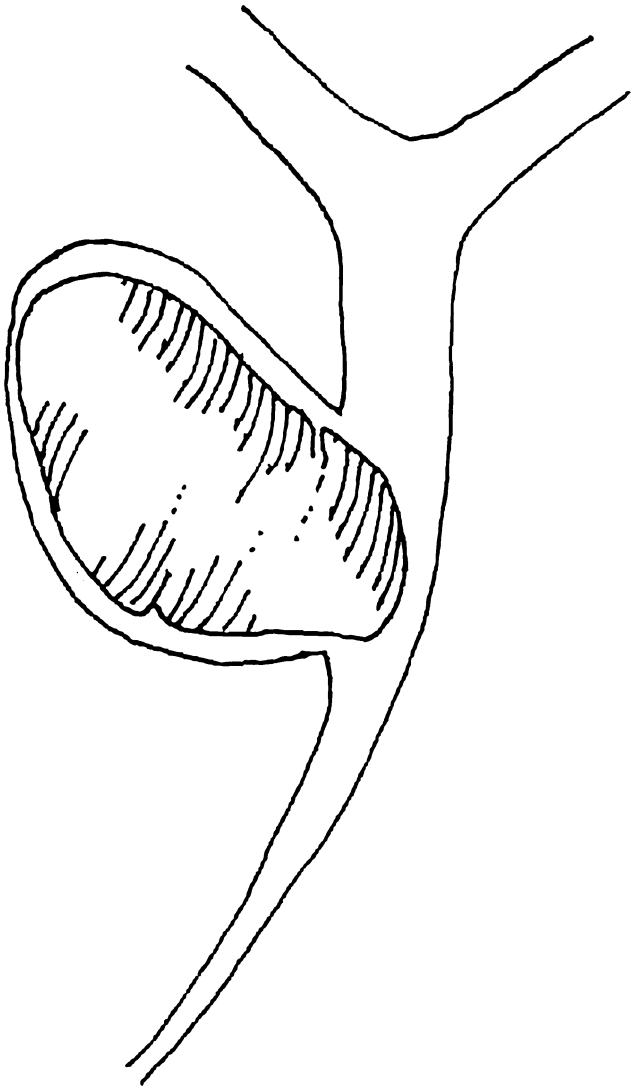

Fig. 3 Mirizzi syndrome type III. A cholecystobiliary fistula involving two-thirds of the circumference of the common bile duct was present in 10 patients (3%). The gallbladder is frequently atrophic whit this type of Mirizzi

case a gastrojejunostomy secondary to duodenal involvement in a complex cholecystoenteric fistula and associated partial cholecystectomy with suture of the stump. Other frequent procedures were partial cholecystectomy, suture of the gallbladder stump, and fistula repair when present. Most patients with Mirizzi IV were repaired with a Roux en Y hepaticojejunostomy (45%), whereas three patients were repaired over a latex T tube.

Sixty-three (19%) patients suffered one or more intraoperative complications–the most frequent were hemorrhage from the gallbladder bed, injury to adjacent organs (stomach, duodenum, and colon), and biliary tree injuries (Table 5). Postoperative complications developed in 110 (34%) patients; common complications were residual common bile duct stones, pneumonia, and deep venous thrombosis. Severe complications related to the surgical procedure were septic abdominal collections and biliary complications (Table 6). Mortality was 4%; there was an increasing mortality parallel to the severity of Mirizzi syndrome. The histopathology reported 216 (66%) cases of chronic cholecystitis, 67 (20%) cases of acute cholecystitis, and 44 (14%) cases of atrophic gallbladder.

Discussion

Reported incidence of cholecystoenteric fistula ranges from 0.15% to 4.8% [3], whereas for Mirizzi syndrome it is approximately 1% (0.3% to 1.4%) [7–9]; however, these are figures from Europe and the United States of America, which we do not believe reflect the reality of other regions of the world. For example, a recent study from Mexico

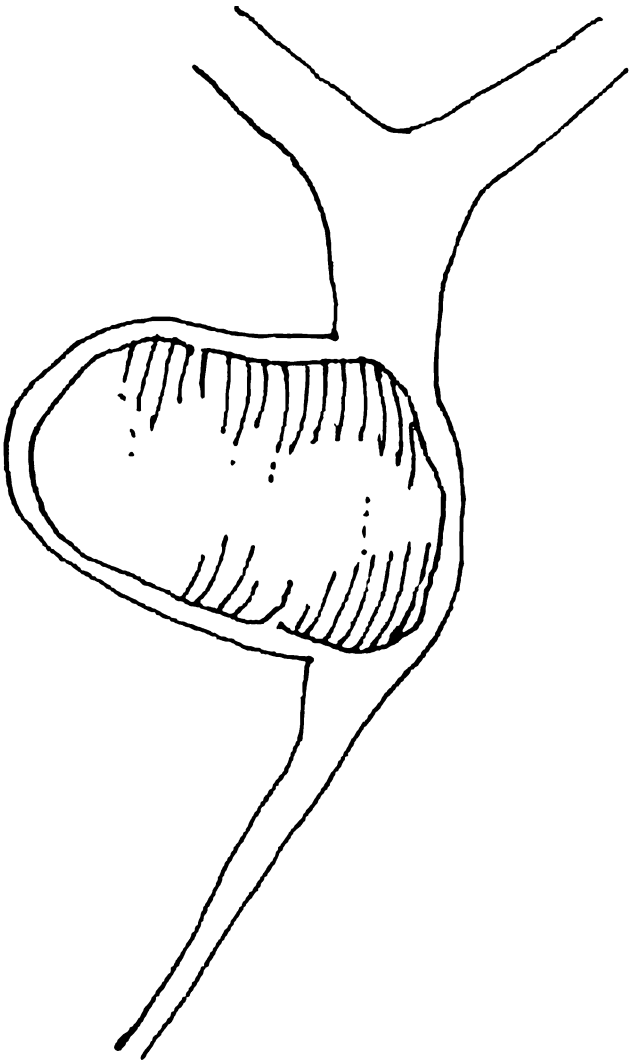

Fig. 4 Mirizzi syndrome type IV. A cholecystobiliary fistula comprising the whole circumference of the common bile duct was present in eight patients (2.4%). Similar to Mirizzi type III, the gallbladder is frequently atrophic

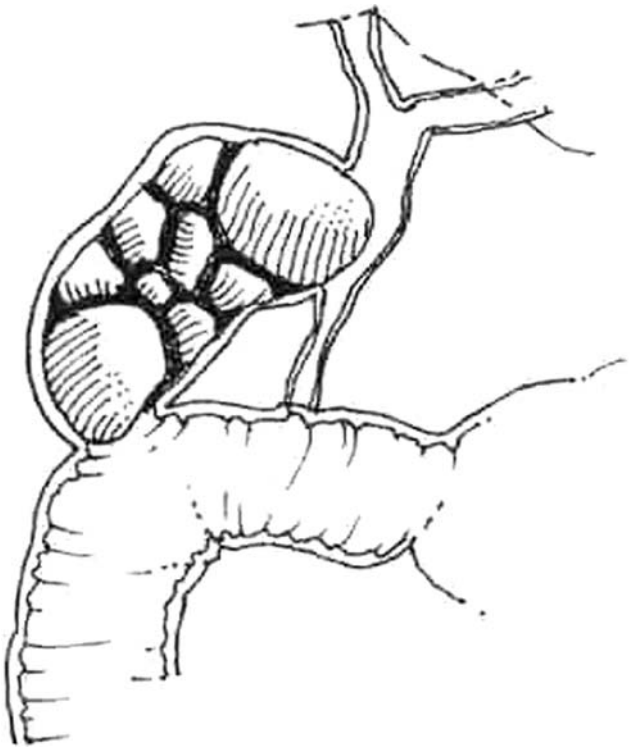

Fig. 5 Mirizzi syndrome type V. Corresponds to any type of Mirizzi associated with a cholecystoenteric fistula without gallstone ileus. This condition was present in 94 patients (29%)

reported an incidence of 4.7% for Mirizzi syndrome in 442 patients [10]. The present series, from a community hospital located in a rural region of South America, shows a higher incidence of Mirizzi syndrome (5.7%) and an incidence of cholecystoenteric fistula of 1.8%, similar to the reported incidence [3, 11]. Few articles have described the coexistence of Mirizzi syndrome and cholecystoenteric fistulas [2, 3, 6, 12]; however, we have noticed this rare and severe complication with some frequency in our patients,

Table 5 Intraoperative complications and findings

Complication	Mirizzi I ($n = 170$)	Mirizzi II ($n = 76$)	Mirizzi III ($n = 61$)	Mirizzi IV ($n = 20$)	Total ($n = 327$) (100%)
None	155	51	45	13	264 (81)
Hepatic artery injury	4	–	1	2	7 (2)
Gastric injury	3	4	1	–	8 (2.4)
Duodenal injury	–	5	3	–	8 (2.4)
Colonic injury	1	1	1	–	3 (0.9)
Gallbladder bed hemorrhage	7	5	3	–	15 (4.5)
Common hepatic duct injury	–	5	1	2	8 (2.4)
Common bile duct injury	–	1	3	–	4 (1.2)
Hepatic confluence injury	–	–	1	2	3 (0.9)
Right hepatic duct injury	–	1	1	–	2 (0.6)
Atypical anatomy	–	3	1	1	5 (1.5)

Table 6 Postoperative morbidity and mortality

Type of complications	Mirizzi I ($n = 170$) (%)	Mirizzi II ($n = 76$) (%)	Mirizzi III ($n = 61$) (%)	Mirizzi IV ($n = 20$) (%)	Total ($n = 327$) (100%)
None	139 (81.7)	51 (67)	24 (39.3)	3 (15)	217 (66)
Medical[a]	18 (10.5)	11 (14.5)	9 (14.7)	3 (15)	41 (12.5)
Deep venous thrombosis	5 (3)	3 (4)	17 (28)	4 (20)	29 (8.8)
Residual common bile duct stones	18 (10.5)	11 (14.5)	8 (13)	–	37 (11.3)
Septic abdominal collections[b]	7 (4)	7 (9)	7 (11.4)	3 (15)	24 (7.3)
Wound infection	8 (4.7)	3 (4)	12 (19.6)	4 (20)	27 (8.2)
Biliary stricture	0	1 (1.3)	7 (11.4)	3 (15)	11 (3.4)
Other biliary complications[c]	0	7 (9)	4 (6.5)	4 (20)	15 (4.6)
Other complications[d]	1 (0.6)	9 (12)	1 (1.6)	4 (20)	15 (4.6)
Mortality	1 (0.6)	3 (4)	5 (8)	4 (20)	13 (4)

[a] Medical: acute myocardial infarction, pneumonia, postoperative ileus

[b] Septic abdominal collections: subphrenic abscess, hepatic abscess

[c] Other biliary complications: biliary fistula, cholangitis

[d] Other complications: hemoperitoenum, evisceration, gallstone ileus

leading us to suggest the association of these two conditions [2].

Mirizzi syndrome develops in patients with longstanding gallstone disease; however, the range of age for presentation varies from 22 to 95 years or older with a mean age of 48 to 61 years. Female patients are affected more frequently than men [5–9]. Patients with cholecystoenteric fistula also present in the sixth decade of life (age range, 13–97 years) and also are more common among women [3, 12–17]. In this study, these characteristics were similar; our patients were mostly women suffering from gallstone disease for 20 or more years. Mirizzi syndrome type I was the most frequent type in our patients, by definition this type of Mirizzi consist on the extrinsic compression of the common bile duct due to an impacted gallstone in the cystic duct [4–6]; this condition is not so rarely present in patients with acute cholecystitis [5, 18, 19]. The inflammatory process associated to acute cholecystitis could be considered the first step of the development of Mirizzi syndrome. If this process persists and becomes chronic, the gallstone eventually could erode the common bile duct and the other types of Mirizzi syndrome would develop [2, 4, 5].

The cause of gallstone ileus is an impacted gallstone in some part of the bowel, most frequently in the ileum at the ileocecal valve [2, 3, 12–17]. Gallstones pass to the bowel through a cholecystoenteric fistula. Frequently when cholecystectomy was performed at a late stage of this disease, a shrunken gallbladder without gallstones, with a wide communication with the common bile duct, choledocholithiasis or bile duct stricture, and the cholecystoenteric fistula healed were found [3, 13]; all of these findings represented different types of Mirizzi syndrome. In this series only 12 patients with cholecystoenteric fistula and Mirizzi syndrome presented with gallstone ileus, and in most of them the procedure performed was an enterolithotomy. Only in two patients a complete procedure, including cholecystectomy and closure of the fistula, was performed: in one of these patients, we identified a Mirizzi syndrome type II [2] and in the other a Mirizzi IV. In this study, we found a strong association of cholecystoenteric fistula with Mirizzi syndrome according to the initial Csendes et al. [5] classification. Patients with higher types of Mirizzi are more frequently associated to cholecystoenteric fistula; the reason for this association is that Mirizzi types II, III, or IV represent a more advanced and chronic inflammatory process in the gallbladder area and consequently adjacent viscera are at a higher risk of become involved in the inflammatory process and develop a fistula [2, 6]. The new classification proposed by Csendes et al. [6] addresses this clinical scenario by the addition of a fifth type. According to this classification, we found that patients with Mirizzi syndrome type V constitute the second most common type of this condition. This fact supports the concept of two-stage surgery in patients with gallstone ileus and also drives our attention toward a more careful dissection of the gallbladder and particularly of the Calot triangle whenever a Mirizzi syndrome is diagnosed in the preoperative study or during surgery.

The heterogeneity of surgical procedures in this series could be explained by the wide period of time for which these patients were treated (13 years), and the different surgeons who operated on these patients. We also must consider the unexpected surgical findings and the limited resources available at our institution. However, in most patients with Mirizzi I we performed a simple

cholecystectomy with or without IOC. Patients with Mirizzi II, III, or IV underwent more complex operations due to the disturbed anatomy of the triangle of Calot. Most patients with Mirizzi II and III had a partial cholecystectomy and suture repair of the gallbladder stump. In 9 of 20 patients with Mirizzi IV, a hepaticojejunostomy was constructed. These surgical interventions were in accord with the accepted published procedures for Mirizzi syndrome [5–10]. The rate of intraoperative complications and the type of complications that we experienced with our patients confirm the severity of the chronic or acute inflammation of the gallbladder and the consequent disturbed anatomy of the Calot triangle. Postoperative complications and mortality are within the expected rates and increase according to the severity of the cholecystobiliary fistula [3, 10, 12, 17, 18]. In 260 (79.5%) cases, the histology reported chronic or atrophic changes of the gallbladder, which relates to the chronic characteristic of this condition.

The current laparoscopic approach to most patients with gallstone disease constitutes the main reason why patients with suspected acute or chronic complications of gallstone disease, such as Mirizzi syndrome, must be carefully studied before surgery. Some authors support the open approach for patients with suspected Mirizzi syndrome [12, 19], whereas others propose the laparoscopic approach, which is more difficult and has a higher risk of bile duct injury. However, the laparoscopic approach in expert hands with the appropriate technology seems to be safe [12, 20]. We believe that the open approach of patients with suspected Mirizzi syndrome or cholecystoenteric fistula is safer in our institution and probably in most institutions of developing countries, where access to diagnostic technology, such as magnetic resonance cholangiography, endoscopic retrograde cholangiopancreatography on daily basis, the use of intraoperative ultrasonography, or surgical technology, such as choledoscopy or laparoscopic staplers, are not available.

Conclusion

Patients in whom Mirizzi syndrome is suspected on abdominal ultrasonography must be cautiously approached. When during surgery for gallstone disease a cholecystoenteric fistula is encountered, the possibility of an associated Mirizzi syndrome must be considered. The findings of this study confirm the association of Mirizzi syndrome with cholecystoenteric fistula and support the new proposed classification.

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