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SURGICAL ENDOSCOPY and Other Interventional Techniques

Bile duct injuries: management of late complications

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Abstract
Background: Laparoscopic cholecystectomy is the treatment of choice for gallbladder stones. In the current study, this approach was associated with a higher incidence of biliary injuries. The authors evaluate their experience treating complex biliary injuries and analyze the literature.
Methods: In a 15-year period, 169 patients with bile duct injuries (BDIs) resulting from open and laparoscopic cholecystectomies were treated. The patients were retrospectively evaluated through their records. Biliary injury and associated lesions were evaluated with imaging studies. Surgical management included therapeutic endoscopy, percutaneous interventions, hepaticojejunostomy, liver resection, and liver transplantation. Postoperative outcome was recorded. Survival analysis was performed with G-Stat and NCSS programs using the Kaplan–Meier method.
Results: Of the 169 patients treated for BDIs, 148 were referred from other centers. The injuries included 115 lesions resulting from open cholecystectomy and 54 lesions resulting from laparoscopic cholecystectomy. A total of 110 patients (65%) fulfilled the criteria for complex injuries, 11 of whom met more than one criteria. Injuries resulting from laparoscopic and open cholecystectomies were complex in 87.5% and 72% of the patients, respectively. The procedures used were percutaneous transhepatic biliary drainage for 30 patients, hepaticojejunostomy for 96 patients, re-hepaticojejunostomy for 16 patients, hepatic resection for 9 patients, and liver transplantation projected for 18 patients. Hepaticojejunostomy was effective for 85% of the patients. The mean follow-up period was 77.8 months (range, 4–168 months). The mortality rate for noncomplex BDI was 0%, as compared with the mortality rate of 7.2% (8/110) for complex BDI. Mortality after hepatic resection was nil, and morbidity was 33.3%. The actuarial survival rate for liver transplantation at 1 year was 91.7%.
Conclusions: Complex BDIs after laparoscopic cholecystectomy are potentially life-threatening complications. In this study, late complications of complex BDIs appeared when there was a delay in referral or the patient received multiple procedures. On occasion, hepatic resections and liver transplantation proved to be the only definitive treatments with good long-term outcomes and quality of life.

Key words: Bile duct injury — Late complication — Management

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Currently, laparoscopic cholecystectomy is the treatment of choice for gallbladder stones. From the beginning, this approach was associated with a higher incidence of biliary injuries than the open procedure. The incidence of such injuries ranged between 0.3% and 1.3% in the 1990s [1–3], and currently stands at about 0.6%. The injuries resulting from laparoscopic cholecystectomy seem to differ from those associated with the open procedure. Laparoscopic injuries are more proximal in the bile duct, have an associated thermal mechanism, and are vascular injuries in most cases. Besides, a high percentage of these injuries coexist with biliary fistula, a fact that conditions the small caliber of the bile duct. This obscure picture could worsen if the attending surgeon does not make the correct decision once the bile duct injury (BDI) occurs.

The nonspecialized hepatopancreatobiliary (HPB) surgeon should consider most BDIs to be complex. Surgeons specialized in HPB surgery obtain better results in the treatment of this pathology than nonspecialized surgeons. Thus, this unpleasant situation for patients and doctors could be avoided if the treatments were provided primarily by HPB specialists. For the best management of these complex injuries, the approach should be multidisciplinary, the joint work of surgeons, interventional radiologists, and endoscopists.

A complex BDI represents an intricate disease difficult to diagnose and eventually treat. We aim to report

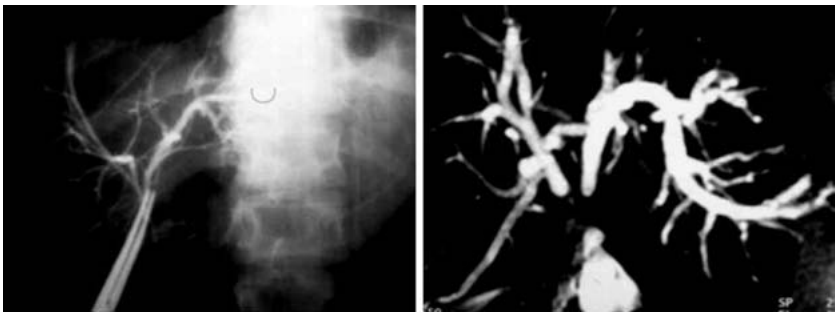


Fig. 1. Intraoperative cholangiography and Cholangio MRI showing a CBD injury that involves the confluence.

our experience with the management of complex BDIs and their late complications, and to analyze the international literature.

Patients and methods

Between January 1989 and December 2004, 169 patients with BDIs (secondary to open and laparoscopic cholecystectomy) were treated in our HPB and Liver Transplantation Unit. Only 21 of these injuries were inflicted in our institution, whereas 148 were referred from other centers.

All the patients were retrospectively evaluated. The information regarding primary operative procedure, intraoperative cholangiography, presenting symptoms, type and level of biliary tract injury, diagnostic procedures, and therapeutic interventions before and after referral was obtained from patients' records.

The level and extent of biliary injury as well as associated lesions (i.e., vascular injuries) were determined by endoscopic retrograde pancreatocholangiogaphy, percutaneous transhepatic cholangiogaphy, ultrasound, computed tomography (CT) scan, cholangio magnetic resonance imaging, and/or angiography, as necessary.

Abdominal angiography was performed if a vascular lesion was suspected because of either an abnormality in the previous studies or a background of any bleeding accident during the cholecystectomy.

We considered the following complex BDIs: those that involved the confluence, those that involved previous failures in repair attempts, any BDI associated with vascular injury, and any biliary injury associated with portal hypertension or secondary biliary cirrhosis (Fig. 1).

All the patients who fulfilled the preceding criteria were included in this study. The surgical management of these patients was defined according to protocols that included therapeutic endoscopy, percutaneous interventions, hepaticojejunostomy, liver resection or liver transplantation depending on the type and level of the BDI, and the presence of complications such as cholangitis, abdominal collections, liver abscess, lobar atrophy, secondary biliary cirrhosis, and portal hypertension.

If the injury was not identified during the primary procedure, the definitive surgical treatment performed 6 to 8 weeks after the bile duct lesion was aimed at avoiding the peak of the inflammatory phenomenon. We used percutaneous transhepatic biliary drainage only if cholangitis or biliary fistula existed to stabilize the patient and to improve local conditions.

Postoperative outcome and complications were recorded. The long-term evolution was followed up using information from the outpatients' record charts. Survival analysis was performed with G-Stat (version 2, Glaxo Smith Kline SA, Tres Cantos, Madrid, Spain) and NCSS Statistical Program (Kaysville, UTA, USA) using the Kaplan–Meier method.

Results

In a 15-year period, 169 patients with BDIs were treated. In our own series of 6,107 laparoscopic cholecystectomies, the incidence of BDIs was 0.14% (9 patients), whereas in the open era (6,265 open cholecystectomies), our incidence of BDIs was 0.19% (12 patients). This is the opposite of what is reported in the literature, possibly due to the exhaustive selection of patients during the learning curve in the 1990s and the supervision by senior surgeons of the surgeries performed by residents and fellows.

Table 1. Patients with complex bile duct (CBD) injuries according to the cause

Lesion involving the hepatic confluence	54
High stenosis with unsuccessful repair attempts	39
Associated vascular injuries	9
Portal hypertension or secondary biliary cirrhosis	19

Of the 169 patients, 92 were women. The mean age of the patients was 46.2 years (range, 6–74 years). Of the 169 injuries, 115 occurred during open cholecystectomy and 54 occurred during laparoscopic cholecystectomy. The injuries were recognized during the surgical primary procedure in 39 cases (23%) and unrecognized in 130 cases (77%). Only 35 patients (21%) had intraoperative cholangiography. A total of 110 patients (65%) fulfilled the criteria for complex injuries, 11 of whom met more than one criteria (Table 1).

The lesions produced during laparoscopic cholecystectomies were complex in 87.5% of the cases, mainly due to the level of the lesion and associated vascular injury, whereas 72% of the injuries that occurred during open surgery were complex due to the level of the injury and the failure of previous treatments. A serious thermal mechanism was associated with BDI in 17 patients.

The procedures used to treat these complex lesions were as follows (we consider only the treatment that solved the symptoms although most patients received more than one procedure): percutaneous transhepatic biliary drainage was used for 36 patients and balloon dilation for all the patients except one treated with an autoexpandable metallic prosthesis. Three patients who had Strasberg types C and E5 lesions (the latter with an associated vascular injury) were treated after failure of hepaticojejunostomy with balloon dilation.

In 90 cases, hepaticojejunostomy was performed for patients with no bilioenteric continuity or as a primary treatment for duct stenosis. Rehepaticojejunostomy was performed for 16 patients after failure of the previous anastomosis.

Hepatic resection was performed for nine patients (7 right hepatectomies and 2 left hepatectomies). These patients represent only the 0.8% of the total liver resections (n = 1,029) performed during the same period. According to Frattaroli's classification [4] of BDIs, four of nine patients had type 5 injury, three had type 6 injury, and two had type 7 injury.

Table 2. Number of patients according to definitive treatment

Procedure	No. of patients
PTBD	36
Hepaticojejunostomy	90
Re-hepaticojejunostomy	16
Hepatic Resection	9
Included in List for Liver Transplantation	18

Of the 19 patients with portal hypertension, 18 were included on the waiting list for liver transplantation. A hepaticojejunostomy was performed with a good outcome for the remaining patient. Of the 18 patients, 14 received transplants, whereas 4 patients died waiting for an organ. These 18 patients represent only 2.8% of the patients (18/508) who received transplants in our unit during the same period (Table 2).

The mean overall follow-up period for this series was 77.8 months (range, 4–168 months). The mortality rate for the group with noncomplex BDIs was 0%, whereas the mortality rate for the group with complex BDIs was 7.2% (8/110). Four of these eight patients died while on the waiting list for a liver transplant. Two patients died after their liver transplant at 1 and 18 months, respectively. Another patient died of a bleeding complication, and the remaining patient died of multiple organ failure.

The overall effectiveness of hepaticojejunostomy as primary treatment for complex BDIs was 85% (76/90). The effectiveness of treatment for high stenosis with previous unsuccessful repair attempts was 93% (15/16). The effectiveness of percutaneous dilation for biliary stenosis was 47% (17/36).

The mortality rate after hepatic resection was nil, and the morbidity rate was 33% (3 of 9 patients with subphrenic abscess, biliary collection, and wound infection, respectively). The mortality rate for the patients on the liver transplant waiting list was 22%. The actuarial survival rate for liver transplantation at 1 year was 92%.

Discussion

In the 1990s, laparoscopic cholecystectomy became the treatment of choice for symptomatic gallbladder stones. This approach resulted in a higher incidence of BDIs. The rate of injuries inflicted during laparoscopic cholecystectomy ranges from 0.3% to 1.3% [1–3]. If a BDI occurs, first attempts to solve this situation are carried out by the surgeon, who usually is not an HPB specialist. These patients often receive multiple treatments that eventually fail and thus increase morbidity [5, 6].

The delay in the definitive treatment at a referral center leads to the development of severe early and late complications. This report focuses on late complications including stenosis of hepaticojejunoanastomosis, lobar atrophy, and secondary biliary cirrhosis and portal hypertension.

Stenosis of hepaticojejunoanastomosis

Certain factors lead to the failure of the first repair attempt, especially a hepaticojejunoanastomosis. These factors are associated with those previously defined as complex BDIs.

Huang et al. [7] analyzed different factors that could predict long-term outcomes after surgical repair. He found statistical significance only for perioperative inflammation ($p = 0.04$) and primary repair performed by a nonreferral surgeon ($p = 0.02$). These authors also stated that serum alkaline phosphatase levels higher than 400 IU at postoperative month 6 predict long-term nonsuccess. For this reason, these patients should be treated as early as possible using therapeutic endoscopy or interventional radiology.

As Smadja [8] stated, it is important to give the patient the best treatment for his problem from the very beginning. Each reanastomosis requires a higher dissection in the pedicle, with subsequent damage to the vascularization of the bile duct. Alan Koffron et al. [9] reported that 61% of patients with biliary injuries for whom the primary repair attempt failed had an associated vascular lesion. The higher the stenosis was, the greater the incidence of vascular associated lesions: 71% for Bismuth type 4, 63% for Bismuth type 3, and 33% for Bismuth type 2.

If an associated arterial injury is suspected, we routinely perform an arteriography before treatment of the complex BDI. The biliary duct is extremely sensitive to arterial blood supply deprivation. Bile duct irrigation originates from two sources: the right and left hepatic arteries above (with bridges between them called the hilar plexus) and the marginal arteries that come from the posterosuperior pancreatoduodenal artery below. They ascend alongside the common bile duct in 3, 9, or 12 o'clock position depending on whether they are 1, 2, or 3 arteries respectively [5, 10]. When a biliary injury occurs just below the hepatic confluence and the right hepatic artery is also injured, the blood supply to the right hepatic duct is maintained through the hilar plexus, which is fed from the left hepatic artery [11] (Fig. 2).

There still exists some controversy regarding the consequences and implications of the association between a BDI and an arterial injury. Alves et al. [12] stated that 19 of 43 patients with biliary injuries had an associated right hepatic arterial lesion. All these patients underwent a Roux-en-Y hepaticojejunostomy. The authors found no differences in terms of intraoperative management, blood consumption, postoperative complications, or outcome in the long-term follow-up period (mean, 56 ± 23 months) between patients with and those without vascular injuries.

If the arterial occlusion has an attritioned distal end, manifests no retrograde flow preventing reconstruction, and coexists with good portal flow and no evident lobar ischemia, then a hepaticojejunostomy can be performed because many patients have a good evolution. On the other hand, if arterial reconstruction is impossible because of technical reasons and lobar ischemia is evident, hepatic resection is indicated together with a hepaticojejunostomy for the remaining duct [13–15].

For the repair of a bile duct stenosis, the Hepp–Couinaud approach [16, 17] to the left duct is good for the left-side lesions or those in which the bile duct confluence is intact. On the other hand, when the ste-

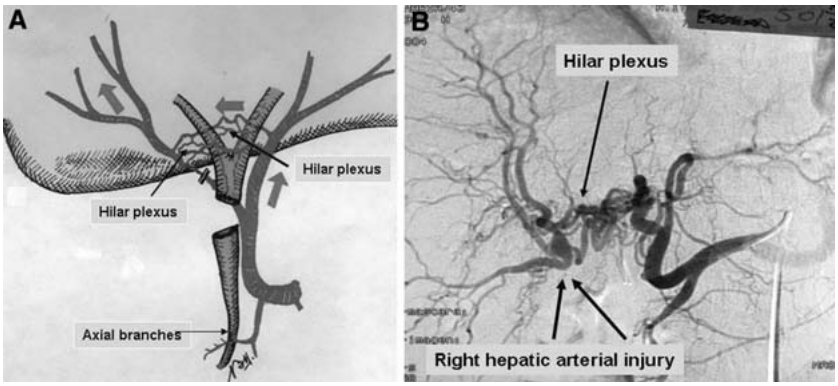


Fig. 2. Revascularization of the right liver from the left hepatic artery. A: Cartoon
B: Angiography.

nosis goes deep in the liver and isolates the right and left ducts, the approach through the gallbladder plate described by Strasberg et al. [18] is an excellent one.

Sometimes it is necessary to perform a liver resection. In our series, this procedure represented only 0.8% of all the liver resections and 5.3% of the BDIs during the same period. Belghiti et al. [19] described the following indications for this procedure: injuries from the confluence or higher with unilateral portal injury, right pedicle destruction, and parenchyma atrophy secondary to a BDI. Majno et al. [20] and Madariaga et al [21] included liver-infected necrosis as an indication.

Among multiple classifications of BDIs (e.g., Bismuth, Strasberg), Frattaroli et al. [4] described the only one that takes into account intrahepatic strictures that stratifies patients who need a hepatic resection to resolve a complex BDI.

The series of Belghiti et al. [19] had no mortality, but showed a high morbidity rate (45%) and a longer hospital stay than found among patients who underwent a hepatectomy for other reasons [19]. We also had no mortality with liver resection, but the morbidity rate was 33%, mainly secondary to infectious disease. Table 3 shows the algorithm we propose for the management of late biliary stenosis.

Table 3. Algorithm for the management of late biliary stenosis

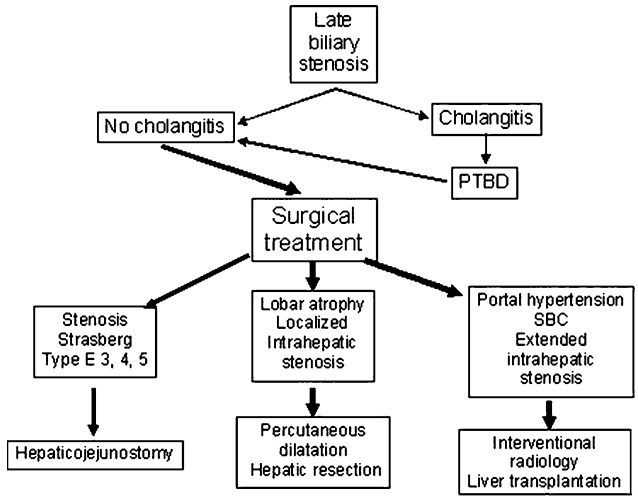
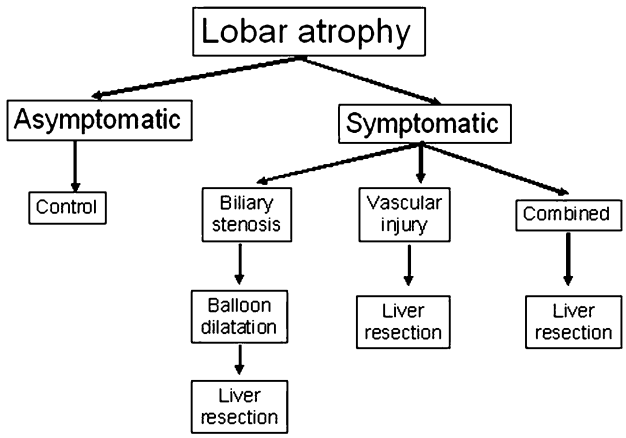


Table 4. Algorithm for the management of lobar atrophy



Lobar atrophy

Lobar atrophy is the end-stage evolution of unilateral injury, usually involving the right lobe. Blumgart [8] proposed three etiologies for this problem: (1) unilateral vascular injury, (2) unilateral biliary stenosis, and (3) 1 and 2 combined. The association between vascular and biliary injury after a laparoscopic cholecystectomy is described earlier. For the management of patients with a complex BDI, when a lobar atrophy is detected, the algorithm presented in Table 4 is proposed.

Secondary biliary cirrhosis and portal hypertension

Successive failures of therapeutic procedures or inappropriate treatment of cholestasis and infection may lead to end-stage liver disease within a few years after the injury [22, 23]. In a historical series of bile duct reconstructions, the incidence of portal hypertension and secondary biliary cirrhosis was 8% [24].

The existence of portal hypertension is a crucial factor in treatment selection for BDIs. In the BDI series of Chapman et al. [6], 23 patients had portal hypertension and the mortality rate for this group of patient was 26%. The mortality rate for the patients with portal hypertension who underwent any surgical procedure was 23% ($n = 5$). In contrast, the mortality rate for the patients without portal hypertension who underwent

any surgical procedure was only 2% ($n = 2$). The patients with complex biliary injuries and portal hypertension who had bilioenteric continuity were treated using interventional radiology in our unit. If this continuity does not exist and the patient has some contraindication for liver transplantation, the bile duct is drained with percutaneous transhepatic biliary drainage, and portal hypertension is treated with a transjugular intrahepatic portosystemic shunt or a mesocaval shunt before bile duct repair. On three occasions, we treated patients with biliary stenosis associated with cavernomatous transformation of the portal vein. These patients had undergone a mesocaval shunt before the hepaticojejunal anastomosis, with a good outcome.

Johnson et al. [25] stated that the development of hepatic fibrosis confirmed by liver biopsy was associated with a delay in the performance of the adequate treatment for patients with biliary stenosis. The presence of cirrhosis during the BDI repair also is considered an ominous sign and the most important risk factor predicting morbidity and mortality increase [26]. Also, the results of biliary reconstruction for these patients with cirrhosis are poor. Pellegrini et al. [27] found good results among only 25% patients with recurrent biliary stenosis associated with biliary cirrhosis. Secondary biliary cirrhosis by itself has a poor prognosis and a high late mortality rate despite the patency of the hepaticojejunostomy [28]. The time required for the development of secondary biliary cirrhosis after benign biliary stenosis is reported to be 7.1 years: 4.6 years for those with common bile duct stones, and 0.8 years for patients with malignant biliary obstruction [29]. Recent studies describe the time of obstruction, the basal alanine aminotransferase (ALT) level, and the time to normalization of ALT level after surgical repair as predictive factors in the development of hepatic fibrosis [30].

Most of the histologic changes produced in the early obstruction stages are reversible if adequate treatment is performed in due time [31]. Unfortunately, many patients present at our unit late after multiple unsuccessful treatments with signs and symptoms of end-stage liver disease. To date, there have been few publications about liver transplantation as a treatment for secondary biliary cirrhosis [5, 21, 32, 33].

In 2002, our experience was published. To the best of our knowledge, it is the largest series published to date [34]. In a 15-year period (1989–2004), 14 patients with secondary biliary cirrhosis received transplants. They represent 2.8% of the 508 patients who received liver transplants at our unit. These figures are higher than those of the European Liver Transplantation Registry, in which liver transplants for secondary biliary cirrhosis represents 1% of all cases. These 14 patients who received transplants fulfilled the indications for liver transplantation because they had an advanced chronic liver disease without any alternative form of therapy or absolute contraindications [35, 36]. The most evident proof of the disease severity experienced by these 18 patients included on the transplant waiting list with secondary biliary cirrhosis was the mortality rate (22%, 4 patients).

The in-hospital mortality rate for the current series was 14.2%, similar to results reported in the literature [31]. One of the patients had an injury of the right arterial and portal pedicle, which led to complete atrophy of that lobe. Intractable ascites, repeated episodes of variceal bleeding, repeated cholangitis, progressive jaundice, pruritus, and poor quality of life all are indicators of the need for liver replacement. The 5-year survival rate for liver transplantation necessitated by benign diseases exceeds 80%, with excellent quality of life. Up to now, we have provided transplants for 14 patients, with an actuarial 1-year survival rate of 91.7%. On the other hand, we have lost four patients on the waiting list, which reflects the disease severity experienced by these patients. Biliary injuries produced during laparoscopic cholecystectomy have proved to be more severe and complex. Short-term results in some cases are poor after repair, whereas concomitant vascular injuries make the situation even worse. All these reasons lead to the suggestion that liver transplantation must be considered within the therapeutic menu for the treatment of these complex lesions.

As we stated previously, liver transplantation is technically more complex because of adhesions, sclerosis of the pedicle, portal hypertension, and coagulopathy. Long-term survival for these patients is similar to that for patients with another pathology. For this reason, liver transplantation is a good therapy for end-stage liver disease in patients with secondary biliary cirrhosis [37].

Conclusions

Complex BDIs after laparoscopic cholecystectomy are potentially life-threatening complications. These injuries must be treated by an HPB surgeon to avoid repeated failed procedures. Despite the different minimally invasive options, the hepaticojejunostomy is the best treatment for these lesions. Late complications of complex BDIs appear when there is a delay in referral or the patient has received multiple procedures. On occasion, hepatic resections and liver transplantation are the only definitive treatments, resulting in good long-term outcomes and quality of life.

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