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Non-Oriental Primary Intrahepatic Lithiasis: Experience with 48 Cases

Paulo Herman, M.D., Telesforo Bacchella, M.D., Ph.D., Vincenzo Pugliese, M.D., André L. Montagnini, M.D., Marcel Autran C. Machado, M.D., José Eduardo M. da Cunha, M.D., Ph.D., Marcel C.C. Machado, M.D., Ph.D.

Department of Gastroenterology, University of São Paulo Medical School, R. Eneas De Carvale Aguar, 255 São Paulo, CEP 05463-900 Brazil

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Abstract. An experience with the diagnosis and treatment of patients with non-Oriental primary intrahepatic lithiasis (PIHL) is described. A group of 48 native Brazilian patients with symptomatic PIHL were studied, and the patients' characteristics, diagnoses, treatment protocols based on the presentation of the disease, prognostic factors, and late results were analyzed. Liver resection was performed in patients with an irreversible lesion, such as parenchymal atrophy or biliary stenosis; and biliary drainage procedures were employed in patients with bilateral disease. Late results were considered good when no postoperative symptoms were observed and poor if there was pain recurrence or cholangitis. Overall good results were observed in 73.4% of the patients. Good late results were observed in 94.1% and 62.1% of the patients with unilateral and bilateral stones, respectively. None of the analyzed parameters (gender, age, previous biliary surgery, bilirubin level, serum leukocyte counts, prothrombin activity, previous history of cholangitis, stone location) predicted poor late results, but the risk for patients with bilateral stones to develop late complications was 7.2 times higher than for those with unilateral disease.Non-Oriental PIHL is a rare disease, and the patients' characteristics are similar to those of patients with Oriental PIHL. We believe that personalized treatment based on the presentation of the disease led to the high incidence of good late results in this series.

The first detailed description of intrahepatic lithiasis was reported by Vachell and Stevens in 1906 [1]. Intrahepatic lithiasis is an uncommon disease, although during the last 20 years an increasing number of publications, especially from the Far East, have appeared in the literature.

Intrahepatic biliary stones may have three distinct ethiologies. (1) The most frequent situation is the migration of gallbladder stones to the hepatic duct and retrogradely into the intrahepatic ducts. (2) Stones can originate in the intrahepatic ducts as a result of biliary stasis secondary to iatrogenic bile duct strictures, choledochal cysts, or biliary stenosis due to benign or malignant disease. (3) Primary intrahepatic lithiasis (PIHL), also known as hepatolithiasis, is rare in the Western world but frequent in eastern Asia, where stones have their origin in the intrahepatic bile ducts although no known cause for their formation has been detected. Here we focus our attention on primary intrahepatic lithiasis, as we were able to diagnose a remarkable number of cases in our institution.

Correspondence to: Paulo Herman, M.D., e-mail: pherman@uol.com.br

Hepatolithiasis occurs most frequently in eastern Asia, where its relative incidence (considering all biliary stone diseases) is 47.3% in Taiwan, 38.0% in China, 17.0% in Korea, 11.7% in Malaysia, and 4.1% in Japan [2]. Reports from the Western world report an incidence of 0.6% to 1.3% [3, 4]. In Latin America, especially in Brazil, there seems to be a relatively high incidence of PIHL, including reports of some cases since the early 1960s [5]. In a recent study, we found an incidence of 2.1% of PIHL among all patients treated for biliary stone disease in our department [6].

The etiology of PIHL is not completely understood. A higher incidence is observed in the Far East, as in Brazil, compared to that in eastern Europe and North America. It is probably due to poor sanitary and nutritional conditions, which seem to predispose to the development of the disease [2, 7]. Hepatolithiasis was a common disease in Japan during the 1950s when diet content was low in fat and protein; but with the economic development and improvement in the quality of life its prevalence is clearly declining in that country [2].

The association of biliary stasis and infection are determinant factors for stone formation. Clinical and experimental data suggest that intestinal bacteria can pass through the portal system into the liver due to bacterial translocation secondary to repeated parasite intestinal mucosal lesions, a common finding in places with poor sanitary conditions. Moreover, it has been observed that biliary infestation by *Clonorchis sinensis* and *Ascaris lumbricoides* can lead to inflammation of the biliary epithelium; moreover, the parasite's fragments or eggs may act as a nidus for stone formation [8].

With the improvements in and the routine use of ultrasonography, diagnosis of liver stones has become more frequent. The most accurate diagnosis is provided by a cholangiographic study, which can be performed percutaneously, endoscopically, or by magnetic resonance imaging.

The treatment of hepatolithiasis includes a multidisciplinary approach, with surgeons, endoscopists, and interventional radiologists participating; but surgery is often required, and sometimes multiple operations are necessary for complete stone clearance. Because of the various presentations of the disease (e.g., location of stones in the intrahepatic ducts, the presence of biliary strictures, liver parenchymal atrophy), surgical treatment

Table 1. Treatment protocol for patients with primary intrahepatic lithiasis.

Diagnosis	Treatment
Unilateral Stones	
Irreversible lesion (biliary stenosis; liver atrophy; nonremovable stones)	Liver resection
Absence of irreversible biliary lesion + intraoperative total stone clearance	Biliary drainage procedure (hepaticojejunostomy/ papilosphincterotomy)
Irreversible biliary lesion + significant dilation of extrahepatic biliary ducts	Resection + biliary drainage procedure
Bilateral Stones	
Absence of irreversible biliary lesion	Biliary drainage procedure
Irreversible unilateral biliary lesion	Resection + biliary drainage procedure
Biliary Cirrhosis/Liver Insufficiency	
Initially paliative treatment	Biliary drainage procedure (sphincterotomy)
Referral to curative treatment	Liver transplantation

must be individualized. Our group has adopted a treatment protocol that is described in this article.

We present our experience with 48 native Brazilian patients with primary intrahepatic lithiasis treated in our department, one of the largest non-Oriental case compilations. We assess patients' characteristics and compare the disease with Oriental hepatolithiasis. We also evaluate our treatment protocol based on the presentation of the disease and it's late results.

Patients and Methods

Between February 1989 and January 1998, a series of 48 patients with PIHL were treated at the Department of Gastroenterology, University of São Paulo Medical School. All patients were native Brazilians from low socioeconomic groups; there were no descendants from Asiatic families. There were 29 females and 19 males ranging from 11 to 75 years of age (mean 39.5 years); 52.1% of them were below age 40 and 77.1% below age 49. All patients were symptomatic and presented with a history of abdominal pain (100%), 46 jaundice (95.8%), 42 fever (87.5%), and 34 chills (70.8%). Altogether, 28 patients (58.3%) had previously undergone biliary surgery in other hospitals, and 5 of them (10.4%) had had more than one biliary surgical intervention.

All patients underwent laboratory, ultrasonographic, and cholangiographic studies as follows: Endoscopic retrograde cholangiography (ERC) was performed when intrahepatic biliary ducts did not present moderate/severe dilation and in the presence of coagulopathy; transparietal cholangiography was undertaken in the presence of dilated intrahepatic biliary ducts. In patients without significant dilation of the biliary three, ERC was indicated owing to the difficulty of accessing a biliary duct percutaneuosly in the absence of dilation. In patients with moderate/severe dilation, biliary stasis is more evident, and there is a high risk of biliary stenosis. In these cases, ERC could give rise to cholangitis due to contamination of the biliary three. Eight patients underwent both procedures to obtain a better evaluation of the biliary tree. Altogether, 21 patients underwent computed tomographic (CT) scan evaluation.

All patients underwent elective surgical treatment. During intraoperative evaluation of the liver parenchyma the presence of atrophy was important for determining the best surgical approach. Intraoperative cholangiography was performed in all patients, and intraoperative cholangioscopy was employed in the last six cases.

Table 2. Surgical procedures in patients with primary intrahepatic lithiasis.

Surgical procedure	No.
Bilateral Stones (n = 51)	
Hepaticojejunostomy	25
Papillosphincteroplasty	2
Hepaticojejunostomy + bisegmentectomy (II, III)	3
Hepaticojejunostomy + left hepatectomy	1
Unilateral Stones (n = 7)	
Segmentectomy (II, III)	3
Left hepatectomy	1
Right hepatectomy	3
Bisegmentectomy (II, III) + Hepaticojejunostomy	3
Left hepatectomy + hepaticojejunostomy	1
Bisegmentectomy (II, III) + Papillosphincteroplasty	2
Hepaticojejunostomy + stone clearance	3
Papillosphincteroplasty + stone clearance	1

The treatment goal was to remove stones and allow an adequate biliary flow. Therefore treatment was individualized according to the presentation of the disease, which gave rise to an algorithm (Table 1) whose rationale is as follows.

1. In the presence of an irreversible lesion, such as parenchymal atrophy or biliary stenosis, the affected part of the liver is resected.
2. For patients with bilateral intrahepatic biliary stones, the most affected side of the liver (with irreversible disease) is resected. Stones are removed from the contralateral side and a biliary drainage procedure (e.g., hepaticojejunostomy) is performed to allow free biliary drainage and the passage of eventual recurrent stones.
3. Patients with unilateral or bilateral disease, in the absence of an irreversible lesion, are submitted to stone clearance and a biliary drainage procedure to allow bile to drain freely and eventually recurrent stones to pass.

Patients with bilateral stones were subjected to the following procedures: hepaticojejunostomy in 25; papillosphincteroplasty in 2; hepaticojejunostomy associated to liver resection in 4. Patients with unilateral disease were subjected to liver resection (7), liver resection associated to hepaticojejunostomy (4), liver resection associated with papillosphincteroplasty (2), and intraoperative stone clearance associated with a biliary drainage procedure (4) (Table 2).

Table 3. Late complications and treatment.

Complication	Treatment
Cholangitis ($n = 6$)	Medical treatment ($n = 3$)
	Percutaneous drainage and stone removal ($n = 3$)
Liver abscess ($n = 2$)	Percutaneous drainage ($n = 2$)
Cholangitis + liver abscess ($n = 3$)	Surgical drainage ($n = 1$)
	Percutaneous drainage ($n = 2$)
Ascites + digestive bleeding ($n = 1$)	Medical treatment ($n = 1$)
Cholangiocarcinoma ($n = 1$)	Liver resection ($n = 1$)

The mean postoperative follow-up was 119 months (52 months to 22 years). The outcome of surgically treated patients was considered good when no postoperative symptoms were present. Results were considered poor when there was pain recurrence or cholangitis.

With the aim of determining independent variables (gender, age, previous biliary surgery, bilirubin level, number of leukocytes, prothrombin activity, previous history of cholangitis, stone location) capable of predicting the occurrence of poor long-term results, Student's *t*-test, Pearson's chi-squared test, and the Cox regression method were employed. Statistical significance was set at 0.05.

Results

Laboratory evaluation showed elevated levels of γ-glutamyl transpeptidase (87.8%), alkaline phosphatase (75.0%), and bilirubin (47.8%), confirming the presence of cholestatic disease. Blood cultures were positive in 44.4% of the cases, and the most commonly isolated microorganisms were *Escherichia coli*, *Morganella morganii*, *Klebsiella sp.*, and *Enterobacter* sp.

Abdominal ultrasonography showed the presence of intrahepatic stones in 41 cases (85.4%). CT was performed in the last 21 cases and showed stones in all of them (100%). After radiologic and intraoperative evaluation, stone location in the biliary tree was bilateral in 31 patients (64.6%) and unilateral in 17 (35.4%); associated extrahepatic stones were observed in 32 patients (66.7%). Only three patients (6.2%) presented with gallbladder stones but it is important to remember that 28 of the patients (58.3%) had been previously subjected to cholecystectomy. Parenchymal liver atrophy was observed in 10 patients (21%) and atrophy associated with liver abscess in 2 (4.2%).

Bile samples were collected for culture in all cases and were positive in 89.5%. The most commonly isolated pathogens were *Escherichia coli* (39.5%), *Pseudomonas aeruginosa* (23.7%), *Klebsiella* sp. (18.4%), *Streptococcus faecalis* (15.8%), *Enterobacter* sp. (13.2%), *Proteus mirabilis* (7.9%), and *Bacteroides fragilis* (2.6%). In 31.6% of the cases infection was polybacterial.

Postoperative complications were observed in eight patients (16.7%), and included wound infection in three, intraperitoneal abcess in one, ascites in one, biliary fistula in one, digestive bleeding in one, and septicemia in one. All patients were treated by a conservative approach, and no reoperations were required. There was no operative mortality.

At long-term follow-up (more than 52 months) 35 patients (72.9%) had had good results and 13 (27.1%) poor results, which included cholangitis recurrence (9), liver abcess (5), ascitis and upper digestive bleeding (1), and cholangiocarcinoma (1). Late complications were treated as shown in Table 3.

Table 4. Late results according to stone location.

Stone location	Good results	Poor results
Bilateral ($n = 29$)	18 (62.1%)	11 (37.9%)*
Unilateral ($n = 17$)	16 (94.1%)	1 (5.9%)

*$p = 0.116$.

Table 5. Cox regression model: independent variables × occurrence of late complications.

Variable	Regression coefficient	p*	Odds ratio
History of cholangitis	0.44	0.63	1.56
Gender (female)	0.23	0.80	1.25
Age	−0.02	0.44	0.97
Previous surgery	−0.11	0.87	0.88
Bilirubin	−0.09	0.62	0.90
No. of leukocytes	1.69	0.66	1.00
Prothrombin activity	−0.06	0.07	0.94
Stone location (bilateral)	1.97	0.14	7.20

*Statistical significance ($p < 0\ 05$).

One patient developed intrahepatic cholangiocarcinoma 3 years after hepaticojejunostomy and underwent right hepatectomy with a good postoperative outcome; two patients died (4.2%), one due to biliary cirrhosis and digestive bleeding 12 months after hospital discharge and the other from septic complications due to cholangitis 93 months after surgical treatment. Late results according to unilateral or bilateral disease are shown in Table 4.

Independent variables tested—gender, age, previous biliary surgery, bilirubin level, number of leukocytes, prothrombin activity, history of cholangitis, intrahepatic stone location—were not able to predict the occurrence of complications (poor results). The Cox regression model was employed to identify any factor capable of predicting poor results. Patients with bilateral stones were at a 7.2 higher risk of poor results than those with unilateral stones; but none of the variables tested significantly predicted that a patient was more prone to complications (Table 5).

Discussion

Despite being a rare disease in non-oriental countries, where it represents less than 2% of all biliary stone diseases, PIHL treatment represents a challenge even for specialized hepatobiliary centers. In the American literature, there are only a few reported cases of PIHL, and all were in Far East immigrants [9]. In Latin America, Yarmuch et al. from Chile reported the PIHL relative incidence as 1.5% among all biliary stone diseases [10]. In 1963 in Brazil, Bove et al. collected the first 20 cases of the disease [5], and in our department PIHL accounted for 2.1% of all biliary stone diseases treated during in the last 10 years [6]. The higher number of cases observed in our series than in other non-Oriental countries, encouraged us to study the disease.

The presence of biliary infection, usually polybacterial, is almost constant in PIHL, with the most commonly isolated pathogens from the intestinal flora. In infected bile, bacteria (especially *Escherichia coli*), produce β-glucuronidase, an enzyme

that deconjugates bilirubin diglucuronide into glucuronic acid and free bilirubin. In the presence of ionic calcium, which is found in normal bile, free bilirubin may precipitate, originating calculi, especially when a nidus is present [11]. Furthermore, malnourished patients may have deficient levels of glucaro-1, 4-lactone, a β-glucuronidase inhibitor normally present in the bile, which activates the deconjugation reaction [12]. Stones are dark, soft, friable concretions of calcium bilirubinate.

Bile stasis associated with infection leads to biliary strictures or liver abscess in one-third of patients [11, 13]. Repeated cholangitis episodes, which characterize the disease, can give rise to irreversible lesions, such as liver fibrosis and parenchymal atrophy. In severe cases, secondary biliary cirrhosis may develop.

The peak incidence is during the third decade of life, a decade earlier than in patients with cholelithiasis. More than 50% of the patients were younger than 40 years. The case of an 11-year-old girl attracted our attention; she presented with a history of 2 years of abdominal pain and 1 year of cholangitis. She was diagnosed as having bilateral intrahepatic stones and gallbladder and common bile duct stones. She was subjected to stone clearance, cholecystectomy, and a Roux-en-Y hepaticojejunostomy. During follow-up she had one crisis of cholangitis that was treated with broad-spectrum antibiotics with a good outcome. She has been followed for 99 months and is doing well. This case represented precocious presentation of the disease.

Males and females are usually affected with equal frequency. Cholangitis is almost a constant finding; and a triad of symptoms—jaundice, fever with chills, right upper quadrant abdominal pain (Charcot's triad)—is present in about two-thirds of the cases. Symptoms may vary from mild uncharacteristic abdominal pain to septic shock.

Physical examination may reveal right upper abdominal tenderness and an enlarged liver. Scars from previous biliary surgeries are observed in 30% to 50% of the patients. With severe, chronic disease, signs of liver insufficiency due to biliary cirrhosis can be observed.

Laboratory evaluation is usually nonspecific, confirming the obstructive nature of the jaundice. Blood cultures are positive in up to 50% of the cases. Abdominal ultrasonography (US) in expert hands can detect more than 90% of intrahepatic stones but cannot identify or localize biliary strictures. It can, however, detect gallbladder and extrahepatic bile duct stones. CT scans may be less sensitive than US in the detection of stones but is useful for detecting parenchymal atrophy [2, 14]; it is also helpful in the diagnosis of liver abscesses and may be a useful, guide for percutaneous drainage. In our series US detected intrahepatic stones in 85.4% of the patients and CT in all of them (100%).

Until recently, cholangiography—percutaneous (PC) or endoscopic (ERC)—provided the most accurate diagnosis, including the location and shape of stones and the site of strictures [2, 15, 16]. The choice between them depended on institutional experience, and sometimes both were used to ensure a good evaluation of the biliary tree. PC and ERC may also be used therapeutically to provide drainage of the infected bile ducts in patients with severe infection while waiting for definitive treatment. Endoscopic stents for the treatment of biliary stenosis were not employed in this series because expandable stents were not available.

During the last fours years, cholangiography performed by MRI became the procedure of choice for biliary tree evaluation of PIHL [17, 18]. In the present series, however, MRI was not employed because it was introduced as a routine procedure in our hospital in 1997. Intraoperative cholangiography with or without cholangioscopy should also be performed to complement study of the biliary ducts. The success of treatment depends on a complete evaluation of the biliary tree [4, 13].

Intrahepatic stones are usually bilateral, and associated extrahepatic bile duct and gallbladder stones are found in 50% and 30% of the cases, respectively [2, 19]. In our series, bilateral stones were observed in 64.6% of cases and associated extrahepatic stones in 66.7%.

The therapeutic approach for patients with hepatolithiasis should be multidisciplinary, involving surgeons, endoscopists, and interventional radiologists. Treatment is initially surgical [2, 8, 15, 19–22] and the goal is to promote decompression of the biliary tree, control any bile infection, and ensure complete stone clearance. Some authors recommend an endoscopic approach for the treatment of all PIHL [23] but most recommend its use only in cases with distal common duct stone obstruction and cholangitis or for the treatment of recurrence [24, 25]. Broad-spectrum antibiotics must be is administered when cholangitis is diagnosed; when a bile culture is available, it is then targeted to the specific microorganism.

Various operative procedures have been proposed for the treatment of PIHL, such as biliary drainage procedures, liver resection, or both. Treatment should be individualized for each patient, based on stone location, the presence of extrahepatic stones, and the presence of biliary strictures or liver atrophy [20]. We adopted a protocol that tailors the surgical approach to each patient according to the former variables.

Hepatic resection is recommended for patients in whom the involved segment or lobe of the liver, which includes biliary stricture and stones, can be completely removed, especially in patients with parenchymal atrophy. This approach in patients with localized disease is followed by good results in 80% to 100% of cases [15, 20, 22, 26–28]. Hepatic resection for the treatment of localized disease led to good results in 94.1% of cases in our study. Mortality rates for liver resection in specialized centers is currently less than 3%; thus even in patients with unilateral disease with no other complication (atrophy or stenosis), resection is indicated.

For patients with bilateral disease, biliary drainage procedures such as hepaticojejunostomy or papillosphincterotomy are recommended. According to the literature, a biliary drainage procedure in conjunction with stone clearance provides good results in 50% to 80% of cases [5, 29, 30]. Patients with bilateral stones but a unilateral irreversible lesion (e.g., liver atrophy or biliary stenosis) should undergo resection of the most affected part of the liver along with a biliary drainage procedure for the remaining parenchyma. Good results were achieved in 62.1% of the patients with bilateral stones in our series.

Patients with severe disease and secondary biliary cirrhosis (Child's B or C) should undergo a biliary drainage procedure and be referred for liver transplantation. One of our patients, who presented with cirrhosis at the time of diagnosis, was treated by endoscopic sphincterotomy; the patient developed digestive bleeding and died while on the liver transplantation list.

Overall good results after treatment of PIHL were 58.3%, 77.0%, 84.0%, 65.0%, and 73.4% in the series of Chen et al., Tsunoda et al., Di Carlo et al. and Wong and our own, respec-

tively [8, 15, 22, 31]. The best results are achieved in patients with localized disease treated by hepatic resection.

None of the parameters analyzed in this study predicted the occurrence of late complications. However, one should be aware that patients with bilateral stones are at a 7.2-fold higher risk to develop late complications than are patients with unilateral stones. For patients with a high risk of stone recurrence who have previously undergone hepaticojejunostomy, some authors employ techniques that allow an endoscopic approach. These techniques include cutaneous hepaticojejunostomy, where the jejunal loop of the bilioenteric anastomosis is located in the subcutaneous tissue on the abdominal wall to allows a future endoscopic approach with a small skin incision [32]. Another technique was proposed by our group: construction of a laterolateral anastomosis between the jejunal loop of the hepaticojejunostomy and the duodenum to allow a future endoscopic approach [33]. For the treatment of recurrence, the transhepatic percutaneous approach has also been employed, with good results. Complete stone clearance is possible in 80% to 90% of cases when combining surgery and postoperative endoscopic or transparietal complementary methods.

An association between PIHL and cholangiocarcinoma has been reported, with the incidence ranging from 2.3% to 10.0% [15, 17, 25, 34]. In our experience, one patient (2.1%) developed an intrahepatic cholangiocarcinoma 3 years after hepaticojejunostomy and underwent right hepatectomy with a good outcome.

Mortality rates vary from 3.1% to 7.6% [20, 32, 35], with the deaths usually due to septic complications (cholangitis or liver abscess) or liver insuficiency in cirrhotic patients. In our series, the long-term mortality rate was 4.3%.

PIHL is a rare disease whose incidence seems to be higher than expected in Brazil. The patients' characteristics are similar to those of patients from the Far East, suggesting a similar etiology. Treatment is complex and should be individualized according to the presentation of the disease. Overall good late results can be achieved in more than 70% of the patients using this approach.

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Invited Commentary

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Henry A. Pitt, M.D.

Department of Surgery Indiana University Indianapolis, Indiana, USA

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Herman and his colleagues (DOI: 1007/s00268-005-7759-3) from the University of São Paulo Medical Center reported 48 patients with "non-Oriental primary intrahepatic lithiasis" (PIHL). All of their patients were natives of Brazil, and none was of Oriental descent (non-Oriental). Their definition of PIHL excluded (1) stones that originated in the gallbladder and (2) stones in association with postoperative strictures, sclerosing cholangitis, choledochal cysts or cholangiocarcinoma. This series is large by Western standards. However, this strict definition may have selected a subgroup of patients who might have been expected to have a relatively good outcome. In addition, the reader is left with the question of the etiology in these Brazilian patients.

In East Asia, where the experience with intrahepatic stones is the largest in the world, many patients have biliary cystic disease or parasites including Clonorchis, Opisthorchis, or Ascaris. Another factor in Asia is the diet, which tends to be high in carbohydrates, especially rice starch, and low in protein. Animal studies in both hamsters and prairie dogs suggest that this "oriental diet" causes pigment stones. In the report from São Paulo, no mention is made of parasites or diet. However, the presumption is that neither of these factors was similar to the situation in East Asia which, again, questions the etiology.

Herman and colleagues performed liver resections in 17 of 48 patients (35%), and 36 patients (75%) underwent hepaticojejunostomy. Postoperative morbidity (17%) and mortality (0%) were excellent. Late deaths occurred in only two patients (4.2%), and follow-up averaged almost 10 years. Good long-term results were achieved in 35 patients (73%); and not surprisingly, results were better ($p = 0.12$) in patients with unilateral (94%) compared to bilateral (62%) disease. In addition, only one patient (2%) developed a postoperative intrahepatic cholangiocarcinoma, and this tumor was resected with a good long-term outcome. Unfortunately, no data are provided on the initial stone clearance rate or on the rate of recurrent stones.

The management of intrahepatic lithiasis remains controversial. Outstanding issues include (1) the role of nonoperative versus operative therapy; (2) the advantages of resection versus bypass; (3) the role of cholangioscopy and lithotripsy; (4) the use of transhepatic stents and access loops; and (5) the prevention or treatment of biliary malignancy. Perhaps 20% of patients with intrahepatic stones can be managed successfully nonoperatively. In general, the percutaneous approach is more successful than the endoscopic approach. Patients with unilateral disease, a low stone burden, and no strictures or "soft" strictures that respond to balloon dilation are most amenable to nonoperative management. However, if more than two or three procedures required, the addition of an operation is probably most cost-effective.

Another area of debate in the management of intrahepatic stones is whether to resect the involved liver or to remove stones and perform a biliary bypass procedure. Most authorities agree that resection is indicated when the disease is unilateral and the segments or lobe are fibrotic or atrophied. Similarly, when the disease is bilateral, resection is not a good option, but liver transplantation is rarely indicated. Thus, the question is whether to resect or bypass when the disease is unilateral and the liver is functional. The arguments for resection are that the recurrence rate is low, and the risk of cholangiocarcinoma (5–10%) is eliminated. The arguments for bypass are that risk associated with the surgery is even less, and and the parenchyma is preserved. With good patient compliance and good interventional radiology collaboration, bypass may be preferred. However, if patient compliance or radiologic expertise are issues, resection is the preferred approach.

In the paper by Herman and colleagues from São Paulo, neither cholangioscopy nor lithotripsy were mentioned. Both of these techniques may be helpful for managing patients with intrahepatic stones pre-, intra-, or postoperatively. Direct visualization of the intrahepatic ducts with a flexible cholangioscope via transhepatic stent tracks may be performed pre- or postoperatively. During surgery, cholangioscopy via the hilar ducts with either a flexible or a rigid cholangioscope is required to ensure the adequacy of stone removal. Having percutaneous transhepatic stents in place preoperatively facilitates this process. In addition, with direct visualization, strictures may be biopsied to rule out malignancy. In a small percentage of patients, the addition of various forms of lithotripsy also may be helpful for removing particularly large stones lodged above a stricture. Having transhepatic stents in place postoperatively, makes follow-up cholangiography and stone removal a straightforward process.

In most reports in the literature, the "success rate" for stone clearance is more than 90%, and the recurrence rate is 10% to 20%. With the "transhepatic team approach" using transhepatic stents pre- and postoperatively, stone clearance has been uniformly achieved, and stents usually are removed within 6 months of surgery when complete stone clearance has been documented. This approach utilized a "standard" Roux-Y hepaticojejunostomy with a large mucosa-to-mucosa anastomosis and a long retrocolic Roux limb. In the hands of an experienced hepatobiliary surgeon, problems with the anastomosis or the jejunum should be rare. In comparison, creation of an access loop for subsequent use by the interventional radiologist may compromise the biliary-enteric anastomosis or flow through the Roux limb. In addition, documentation of stone clearance also may be compromised.

In the report by Herman and colleagues, patients with premalignant lesions such as choledochal cysts and sclerosing cholangitis

were excluded. This patient selection may account, in part, for the low incidence of cholangiocarcinoma (2%). Another key factor regarding the appearance of a biliary malignancy after a biliary bypass procedure is whether biliary infection has been controlled. With complete clearance of stones, proper management of hilar or intrahepatic strictures, and selective use of long-term transhepatic stenting, the risk of malignant degeneration should be minimized.

In summary, the experience from São Paulo reports a good long-term outcome in 73% of patients with a "balanced" resection/bypass approach. Operative morbidity and mortality were excellent, and the incidence of cholangiocarcinoma was low. However, stone clearance was not documented, and results may have been even better if cholangioscopy, lithotripsy, and selective use of transhepatic stents had been employed.