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Clinical significance of intrahepatic biliary stricture in efficacy of hepatic resection for intrahepatic stones

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Abstract: In the Far East, hepatic resection is the definitive treatment for complicated intrahepatic stones (IHS). However, many investigators have reported that the associated intrahepatic biliary stricture is the main cause of treatment failure. A retrospective comparative study was undertaken to clarify the long-term efficacy of hepatic resection for treatment of IHS and to investigate the clinical significance of intrahepatic biliary stricture in treatment failure after hepatic resection performed in 44 patients with symptomatic IHS. The patients were divided into two study groups: group A, with intrahepatic biliary stricture ($n = 28$) and group B, without stricture ($n = 16$). Residual or recurrent stones, recurrence of intrahepatic biliary stricture, late cholangitis, and final outcomes were analyzed and compared statistically between the two groups. The patients were followed up for a median duration of 65 months after hepatectomy. The overall incidence of residual or recurrent stones was 36% and 11%, respectively, in groups A and B. The initial treatment failure rate was 50% in group A and 31% in group B. Intrahepatic biliary stricture recurred in 46% of patients in group A, while none of the group B patients had biliary stricture recurrence ($P = 0.001$). More than two-thirds of the restrictures in group A were identified at the primary site. The incidence of late cholangitis was higher in group A (54%) than in group B (6%) ($P = 0.002$). Three-quarters of the patients with cholangitis in group A had severe cholangitis, that was recurrent, and related to stones and strictures (n = 11). They and 2 asymptomatic patients in group B required secondary procedures done at a median of 12 months after hepatectomy. Final outcomes after hepatectomy with or without secondary management were good in 80%, fair in 16%, and poor in 4% of our 44 patients. Most recurrent cholangitis after hepatectomy in patients with IHS was related to recurrent intrahepatic ductal strictures. Therefore, to be effective, hepatic resection should include the strictured duct. However, with hepatectomy alone it is difficult to clear the IHS or relieve the ductal strictures completely, particularly in patients with bilateral IHS, so perioperative team approaches that include both radiologic and cholangioscopic interventions should be combined for the effective management of IHS.

Key words: intrahepatic bile duct stricture, intrahepatic stones, hepatic resection

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Introduction

Hepatic resection is the definitive treatment for primary intrahepatic stones (IHS) in East Asia, particularly in patients with disease confined to the left lobe.[1–5] The procedure not only removes the source of recurrent infection, both the stones and affected ducts, together with the chronically damaged liver, but can also prevent the most important sequelae, such as cholangiocarcinoma.[2,6] Many investigators[4,5,7] have reported, however, that intrahepatic biliary stricture, which is commonly associated with IHS, is the main cause of the retaining or recurrence of stones, particularly in patients with bilateral ISH[7] requiring reoperation[8] or other multiple additional procedures such as cholangioscopic[8–10] or fluoroscopic percutaneous stone retrieval[5,7,11] during the long follow-up period after hepatectomy. Thus, we performed a retrospective study to clarify the long-term efficacy of hepatic resection and to investigate the clinical significance of intrahepatic biliary stricture in treatment failure or the recurrence of cholangitis after hepatectomy for IHS.

Patients and methods (Table 1)

From July 1986 to October 1996, 51 consecutive patients underwent hepatic resection for symptomatic IHS in the Department of Surgery at Dong Kang General Hospital, Ulsan, Korea. Patients accounted for 5 percents of cases with biliary stones and 44 percent of IHS, operated on during same study period, respectively. Of

Table 1. Patient characteristics

	Group A ($n = 28$)	Group B ($n = 16$)	Total (%) ($n = 44$)
Age in years, median (range)	47 (29–71)	46 (28–70)	46 (28–71)
Sex (M:F)	12:16	4:12	16:28
Previous biliary operation	12	4	16 (36%)
Acute cholangitis*	26 (93%)	12 (75%)	38 (86%)
Location of IHS			
Left lobe	19	14	33 (75%)
Both lobes	9	2	11 (25%)
Mode of operation			
Emergency	6	2	8 (18%)
Elective	22	14	36 (82%)
Operative procedure			
Lateral segmentectomy	16	9	25 (57%)
Left lobectomy	11	7	18 (41%)
Right lobectomy	1	0	11 (2%)

* $P > 0.05$ (group A versus group B)
IHS, Intrahepatic stone

the 51 patients, 7 were excluded from the final study results because of postoperative death ($n = 2$) or incomplete follow-up ($n = 5$). The operative deaths occurred in the early period of this study. The cause of death was hepatic failure in one patient and postoperative hepatic bleeding in the other patient. Thus, we conduced this study on 44 patients. The study group consisted of 16 men and 28 women, with a median age of 46 years (range, 28–71 years). Sixteen patients (36%) had had one or more biliary operations previously, and 38 patients (86%) presented with acute cholangitis on admission. Ultrasonography was performed routinely as the primary mode of diagnosis in all patients, and the locations of stones and intrahepatic biliary stricture or dilatation were usually confirmed by direct cholangiography and computed tomography.

Forty-one patients (93%) were diagnosed correctly and another three cases were detected unexpectedly by intraoperative cholangiography at the time of operation performed for common duct stones. The location of IHS was left side in 33 patients (75%) and both lobes in 11 patients (25%). Extrahepatic biliary stones were also found in 31 patients (70%). Twenty-eight of the 44 patients (64%) had associated intrahepatic biliary strictures, located in left ($n = 21$), right ($n = 2$), and bilateral intrahepatic duct ($n = 5$), respectively. Intrahepatic biliary stricture was defined as a decrease in the diameter of the bile ducts (above the hepatic hilum) relative to the adjacent parts noted on direct cholangiography. Nineteen cases of intrahepatic stricture were associated with unilateral ISH (relative incidence of 58%, 19/33) and nine cases were associated with bilateral ISH (relative incidence of 82%, 9/11).

Hepatic resection was performed when patients had one or more of the following indications; multiple impacted stones ($n = 43$), stones confined to one segment or one lobe of the liver ($n = 34$), atrophy or fibrosis of involved portion of the liver ($n = 30$), intrahepatic ductal stricture ($n = 28$), micro abscess ($n = 11$) or gross abscess ($n = 5$) of involved portion of the liver, multiple large stones palpable on the surface of the involved liver ($n = 13$), and both lobe involvement with predominant left lobe ($n = 9$) or right lobe ($n = 1$). Thirty-six patients (82%) underwent hepatectomy on an elective basis after radiologic investigation was completed, whereas in 8 patients (18%), emergency hepatectomy was performed because of persistent septic cholangitis. Hepatic resection included the left lateral segment in 25 patients, left lobe in 18, and right lobe in 1, and other combined procedures were choledochotomy, in 37 patients, cholecystectomy in 29, transduodenal sphincteroplasty, in 9, and choledochoduodenostomy in 7 patients.

Postoperatively, ultrasonography was performed routinely at least every 6 months for the first 3 years after operation, and additional information was obtained with computed tomography and/or direct cholangiography for patients who showed symptoms of recurrent cholangitis. We defined residual stones as stones in the intrahepatic duct detected on intraoperative and early postoperative tube cholangiography, and recurrent stones as stones detected during the later follow-up period (i.e., 6 months after operation).

The patients were divided into two groups according to presence or absence of associated intrahepatic ductal

stricture: group A, with stricture ($n = 28$) and group B, without stricture ($n = 16$). The groups were statistically comparable in regard to clinical profiles, including the location of stones, indications for operation, operative procedures, and duration of follow-up.

Patients were followed-up for a median duration of 65 months (range, 7–117 months). Duration of follow-up was less than 12 months in only one patient. Two patients died, one of hepatocellular carcinoma at 61 months, and one of stomach cancer at 63 months, after hepatectomy. We included these two patients in the study groups because they had been free of stones until death.

Treatment failure related to retained or recurrent stones, and recurrence of intrahepatic ductal stricture and late cholangitis, and outcomes after secondary management were analyzed and compared between the two study groups, using the χ^2 test or Fisher's exact test, with $P < 0.05$ considered significant.

Results

Residual or recurrent stones

Postoperatively, residual stones were identified in 11 of the 28 patients (39%) in group A, and 5 of the 16 patients (31%) in group B. Recurrent stones were also detected in 3 of the 17 initially stone-free patients (18%) in group A at 15, 20, and 23 months, respectively, but none were detected in group B. Therefore, treatment failure rate (overall, 43%; 19/44) was higher in group A (14/28; 50%) than group B (5/16; 31%), but the difference was not significant ($P > 0.05$).

Residual or recurrent stones were identified in 9 of the 11 patients (82%) with bilateral IHS, and in 10 of the 33 patients (30%) with unilateral (left lobe) IHS after hepatectomy, the difference being significant ($P = 0.004$).

During follow-up, two patients with residual stones in group A showed spontaneous disappearance of the stones and in two patients in group B, the stones migrated into and were found in the common duct.

Thirteen of the 14 group A patients with either residual or recurrent stones had recurrence of intrahepatic ductal stricture (93%) and 11 of 14 (79%) had late cholangitis. Group B patients with either residual or recurrent stones showed neither occurrence of ductal stricture, nor recurrent cholangitis. These differences were strongly significant ($P < 0.0001$ and $P < 0.0001$, respectively). Consequently, even though the initial treatment failure rate after hepatectomy, in terms of stones was not significantly different between the two study groups, stone-related recurrent cholangitis occurred only in group A because of recurrence of intrahepatic stricture (Table 2).

Recurrent intrahepatic ductal stricture

Intrahepatic biliary strictures recurred in 13 of the 28 patients (46%) in group A, but none of the group B patients developed stricture after hepatectomy ($P = 0.001$). Nine cases of stricture were probably incompletely relieved primary ones, recurring in the contralateral duct ($n = 4$), ipsilateral hilar ($n = 3$), both hilar ($n = 1$), ipsilateral hilar and contralateral intrahepatic duct ($n = 1$), respectively. Another four cases were secondary strictures, occurring in the contralateral side and identified at 1, 4, 15, and 23 months, respectively, after hepatectomy. All of the recurrent strictures were associated with residual or recurrent stones. The recurrence

Table 2. Outcomes of hepatectomy

	Group A ($n = 28$)	Group B ($n = 16$)	Total ($n = 44$)
Follow-up; months; median (range)	63 (7–117)	67 (12–112)	65 (7–117)
Residual stones	11 (39%)	5 (31%)	16 (36%)
Recurrent stones	3/17 (18%)	—	3/28 (11%)
Recurrent ductal stricture*	13 (46%)	—	13 (29.5%)
Primary	(9)		
Secondary (contralateral lobe)	(4)		
Late cholangitis**	15 (54%)	1 (6%)	16 (36%)
Mild, transient	(4)	(1)	
Severe, recurrent	(11)	—	
Symptom related to stone and stricture***	11 (39%)	—	11 (25%)
Secondary management	10 (36%)	2 (12.5%)[a]	12 (27%)

* $P = 0.001$ (group A versus group B); ** $P = 0.002$ (group A versus group B); *** $P = 0.003$ (group A versus group B).

[a] Migrated common duct stones, asymptomatic

of ductal strictures was observed in 7 of the 11 patients (64%) with bilateral IHS and in 6 of the 33 patients (18%) with unilateral IHS ($P = 0.007$) (Table 2).

Late cholangitis

Postoperative late cholangitis occurred in 16 patients (36%); 15 in group A, and 1 in group B. It was mild and transient in 5 patients, of whom, in only 1 was it related to stones. In the other 11 patients the cholangitis was moderate to severe and recurrent, and all were in group A ($P = 0.005$) (Table 2). The cholangitis was related to both stone and stricture in 10 patients; in 1, it was suspected of being related to choledochoduodenostomy.

Secondary additional procedures and final outcomes

Secondary procedures were usually performed within 2 months after hepatectomy in patients with residual stones in the central intrahepatic ducts, particularly in the patients with early postoperative cholangitis. Patients with small residual stones in the peripheral intrahepatic ducts were observed and followed up.

Thus, of the 19 patients with initial treatment failure (group A, 14; group B, 5), 10 patients (36%) in group A, with severe recurrent cholangitis and 2 patients (12.5%) in group B, with asymptomatic migrated common duct stone, underwent secondary procedures (Table 2), consisting of either reoperation or radiologic intervention alone, or combined with cholangioscopy at a median of 12 months (range, 2–87 months) after hepatectomy. The remaining 7 patients were excluded from secondary management because 6 patients were asymptomatic and 1 showed good response to conservative treatment. The secondary procedures were selected and combined based on the extent of involvement of the liver and biliary tract, and on the patients' condition (Table 3).

Of the five patients who had reoperation alone, two (left medial segmentectomy and transduodenal sphincteroplasty, respectively) showed no stone recurrence at 21 and 42 months, respectively. Of the other three, one died of septic cholangitis 24 days after surgical drainage of liver abscess, one had mild cholangitis but no stone 77 months after open drainage of delayed subphrenic abscess, and one had incomplete stone removal with recurrent cholangitis, but was alive 92 months after reoperation (this patient refused further treatment).

In patient 4 in Table 3, small stones retained in the left hilar duct stump disappeared after open drainage of delayed subphrenic abscess protruded into the anterior abdominal wall. It was suspected that the stones had been delivered spontaneously through the biliary fistula and abscess cavity.

Four patients underwent fluoroscopic percutaneous stone removal with balloon dilatation via either T-tube or percutaneous transhepatic biliary drainage tract and all were free of symptoms and stone recurrence at 5, 10, 25, and 51 months, respectively after the procedure.

Three patients with the most severe stone complications received multiple procedures, consisting of initial choledochotomy with operative cholangioscopy,

Table 3. Secondary management for residual or recurrent stones ($n = 12$)

Patient	Stones	Stricture	Procedure	Follow-up for stone (months)
1	B4, Lt hilar stump	Lt hilar	Lt medial segmentectomy	No recurrence (21)
2	Common duct	—	Transduodenal sphincteroplasty	No recurrence (42)
3	B6,B7	RP, hilar	Drainage of liver abscess	Died of septic cholangitis (1)
4	Lt hilar stump	Lt hilar	Drainage of delayed subphrenic abscess	No recurrence, mild cholangitis (77)
5	B2,B4	Lt hilar	Repair of biliary fistula	Recurrent stones, alive (92)
6	B6,B7	RP	Fluoroscopic + dilatation	No recurrence (5)
7	B6	RP	Fluoroscopic + dilatation	No recurrence (10)
8	Lt hilar stump	Both hilar	Fluoroscopic + dilatation	No recurrence (25)
9	CBD	—	Fluoroscopic	No recurrence (51)
10	B6,B7	RP, Lt hilar	Choledochotomy + PTCS + EHL + fluoroscopic + dilatation	No recurrence (18)
11	RA,RP	Rt hilar	Choledochotomy + POC + PTCS + EHL+ fluoroscopic + dilatation	No recurrence (19)
12	B5–8	RA,RP	Choledochotomy + PTCS + EHL + dilatation	Recurrent, but asymptomatic (49)

B2, Left lateral posterior branch; B4, left medial branch; B5, right anterior inferior branch; B6, right posterior inferior branch; B7, right posterior superior branch; B8, right anterior superior branch; RA, right anterior branch; RP, right posterior branch; Lt, left; Rt, right; POC, postoperative cholangioscopy; EHL, elctrohydraulic lithotripsy; PTCS, percutaneous transhepatic cholangioscopy; CBD, common bile duct

Table 4. Final outcomes of hepatectomy with or without secondary management for IHS

	Group A (n = 28)	Group B (n = 16)	Total (n = 44)
Good			
Stone and symptom free	22 (79%)	13 (81%)	35 (80%)
Fair			7 (16%)
Stone (+) sx (−)	3	3	
Stone (−) sx (+)	1	—	
Poor			2 (4%)
Stone and sx (+)	1		
Stone-related death	1		

sx, Symptoms of cholangitis

and later multiple sessions of either postoperative cholangioscopy (POC) or percutaneous transhepatic cholangioscopy (PTCS) with electrohydraulic lithotripsy (EHL) for residual stones and/or fluoroscopic percutaneous stone removal with balloon dilatation for recurrent stricture and stones. Two of these patients were free of both symptoms and stones at 18 and 19 months, respectively, while the third patient showed stone recurrence 49 months after initiation of the procedures, but is currently asymptomatic (Table 3).

Thus, of the 44 patients, 35 (80%) had a successful outcome, 1 patient died of stone-related sepsis, and 1 patient showed recurrent cholangitis without stone, while the remaining 7 patients with stones needed further follow-up (Table 4).

Discussion

The present study has clearly shown that intrahepatic ductal stricture associated with IHS continuously influenced recurrence of late cholangitis by way of restricture formation, bile stasis, and ultimate stone recurrence, even after hepatic resection, strongly suggesting a vicious cycle in IHS. The etiology of intrahepatic ductal stricture in IHS remains uncertain. Matsumoto et al.[12] have suggested a congenital origin of stricture. But Wong[13] has suggested that strictures are of inflammatory origin, initiated by exaggeration of the normal healing process, exacerbated by transmural ductal injury by infection and stones. In our study, postoperative stricture formation occurred only in patients with initial stricture. This finding is suggestive of a continuous inflammatory bile duct process, since it may be stimulated regardless of the presence of stones.

As shown in our study, intrahepatic biliary stricture represents a difficult problem in the treatment of IHS because it is a main cause of treatment failure and stone recurrence, not only after conventional surgery,[4,5,14,15] but also after other nonsurgical alternative.[10,11] It occurred in 64% of the patients with hepatectomy (28/44) and in 68% of the treatment failure group (13/19), respectively, in the current study. Generally, three-quarters of patients with IHS have associated intrahepatic biliary stricture in areas of East Asia endemic for IHS.[5,9,16]

There is still controversy in regard to resection of liver when the left lobe is packed with stones and associated with intrahepatic ductal stricture but the involved lobe is grossly normal.[7] In such circumstances, dilatation of stricture with removal of stone only, without resection of the involved liver part is usually followed by restricture formation,[3,9,17] indicating the necessity of performing hepatic resection. There is another controversy in respect of extent of hepatic resection. When the left lateral segment is atrophic but the medial segment is grossly normal, many hepatobiliary surgeons [1–3,5,7] prefer lateral segmentectomy to left lobectomy because the technique is much easier and less time-consuming. However, the current study definitively demonstrated that symptomatic intrahepatic ductal stricture recurred in proximity to the left hilar duct stump after left side hepatic resection in five patients (four with lateral segmentectomies and one with lobectomy). Therefore, left hepatic lobectomy would be warranted if a severe biliary stricture is identified in the left hepatic duct distal to the orifice of the medial segmental duct.

In contrast to left hepatic resection, right hepatic lobectomy is usually avoided because of the high risk involved.[4,5] With recent advances in the percutaneous approach, dilatation therapy has became the preferred method for right lobe IHS with stricture.[5,7] Bilateral IHS, in contrast to unilateral IHS, showed many problems in the current study, since patients with bilateral IHS not only had a higher incidence of associated ductal stricture but also a higher rate of postoperative restricture formation, as well as retention or recurrence of stones, compared with patients with unilateral IHS. Jeng et al.[7] have reported a satisfactory result for bilateral hepatolithiasis with bilateral stricture by performing partial resection of the left lobe and postoperative adjuvant biliary dilatation for the right lobe. They[18] have also suggested prolonged intrahepatic stenting for long segmental stricture to prevent restricture. Recently, we have also adapted the stenting of a large-bore catheter through the stump of the resected left hepatic duct rather than performing T-tube choledochostomy in bilateral hepatolithiasis.

For symptomatic residual or recurrent IHS, surgical reoperation is usually not effective and involves a high risk.[4] In our study, surgical intervention was conducted in eight patients, but the results were satisfactory in only two. The remaining six patients will require another interventional procedure.

Currently, the preferred non-surgical alternatives for residual or recurrent IHS are percutaneous fluoroscopic[7,11,19] or cholangioscopic[8,9,10,20] stone retrieval. Many investigators, however, have also reported that the associated intrahepatic ductal stricture is the most common cause of treatment failure in fluoroscopic[5,11] or cholangioscopic stone removal.[8,10,20]

One Taiwan series[5] has reported a treatment failure rate for stone extraction without dilatation therapy of up to 100%, but with addition of the dilatation, the failure rate was reduced to 5.3%. Other factors also responsible for failure of POC or PTCS are intrahepatic ductal angulation[8] or drainage variation in posterior segmental duct[10] or large impacted stones requiring EHL[4,8,20,21]

Our six patients in whom the fluoroscopic percutaneous approach was employed also required dilatation of the stricture, and, as well, preceding cholangioscopic EHL was required in three for the success of the treatment.

In the past two decades, the reported incidence of residual or recurrent stone after surgery for IHS has been very high, ranging from 48.2% to 77.6%.[2,3,14,15,22] These figures are a little higher than the 43% treatment failure after hepatectomy alone in the current study. Recently, the success rate has been much improved by surgery combined with radiologic and cholangioscopic management, including EHL. Fan et al.[4] achieved 89.8% complete stone clearance rate by a systematic approach and Pitt et al.[23] reported 94% stone-free rate by a transhepatic team approach.

In summary, the 80% final success rate after hepatectomy with or without additional management for IHS in the current study is not satisfactory. We believe that hepatic resection alone is not an effective procedure for the treatment of IHS. Without doubt, we believe that we can achieve better results in future if we perform hepatectomy combined with more liberal and more aggressive use of perioperative cholangioscopy for the removal of both stones and strictures.

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