Hepatolithiasis is a common disease in Southeast Asia, and the relative incidence of hepatolithiasis is 20% in China and Taiwan. However, our study in Japan investigated 105,062 patients with cholelithiasis between 1989 and 1992 and found that 2,333 of these patients (2.2%) had hepatolithiasis. In Japan, the number of patients with hepatolithiasis also is lower compared with previous nationwide statistics. This decrease could be attributable to the fact that as the number of patients undergoing laparoscopic cholecystectomy increased, the size of the patient pool increased, thus lowering the relative incidence of cholelithiasis and hepatolithiasis.

As ultrasonography and computed tomography have come into wider use, it has become possible to not only identify the location of hepatic stones but also assess these stones qualitatively. With magnetic resonance cholangiopancreatography or helical computed tomography, the 3-dimensional structure of the bile duct can now be described; thus, the accuracy in diagnosing hepatolithiasis has been greatly improved. Recent advances in medical technology have been marked, and the results of surgical procedures, such as hepatectomy, have improved. Furthermore, non-invasive treatments, such as percutaneous transhepatic cholangioscopic lithotripsy (PTCSL) and extracorporeal shock wave lithotripsy (ESWL), have been established. However, postoperative residual
PATIENTS AND METHODS

Between January 1, 1971, and December 31, 2000, 2104 patients with cholelithiasis were admitted to Wakayama Medical University Hospital, Wakayama, Japan. Cholecystolithiasis accounted for 78% of the cases, whereas hepatolithiasis accounted for 4% (43 men and 46 women). Patients ranged in age from 20 to 72 years, with a mean age of 56.9 years. Sixty-eight patients (54%) had previously undergone 1 or more biliary procedures. We classified the 89 patients with hepatolithiasis by pathologic types. Based on the location of stones in the hepatic bile duct, patients were grouped into the following types: intrahepatic (type I), extrahepatic (type E), and both (type IE). Based on the lobe localization of hepatolithiasis, patients were grouped into the following types: left lobe (L type), right lobe (R type), and bilateral lobe (LR type).

All patients underwent surgical or nonsurgical intervention, and the presence of hepatolithiasis was confirmed. In terms of the treatment procedures, 34 patients (38%) underwent hepatectomy; 36 (40%), cholangiointerostomy (choledochojunctionostomy or cholangiointerostomy); 12 (13%), T-tube insertion; and 7 (8%), PTCSL. Intraoperative cholangioscopy (external diameter, 4.9 mm; CHF-P20; Olympus, Tokyo, Japan) was routinely used instead of intraoperative cholangiography for visualizing the residual stones, ductal strictures, and tumors. Postoperative cholangiography and cholangioscopy were routinely performed to detect residual stones. In cases treated by PTCSL, a cholangioscope was inserted through the percutaneous transhepatic cholangiodrainage (PTCD) fistula orifice, where grasping forceps could be inserted through the cholangioscope to remove any stones. Giant and impacted stones were fragmented by introducing an electrohydraulic shock wave lithotripter probe or pulsed dye laser before 1997, but were fragmented by introducing holmium (Ho):YAG lasers after 1998. We established the following treatment conditions: 0.8 J, 20 Hz, and 16 W. Under these conditions, 1-cm stones can be pulverized in 10 seconds. Also, board-shaped stones can be sufficiently pulverized without inducing hemorrhage from the bile duct wall.

In combination with other treatments such as PTCSL, ESWL is performed on patients with intractable hepatolithiasis, such as IE and LR types, in whom hepatectomy would not be sufficient for complete remission. We used a lithotripter (Lithostar 2-plus lithotripter; Siemens Inc, Erlangen, Germany). Under imaging guidance via PTCD or an endoscopic nasal bile draining tube, we established the maximum voltage and shot count as 19 kV and 4000 times, respectively, and we performed irradiation 1 to 10 times. The lithotripter is equipped with ultrasonography and x-ray modes. Although ultrasonography is affected by gastrointestinal gas, pneumobilia, and subcutaneous fat thickness, tests can be performed using the lithotripter regardless of these conditions. We analyzed chronological changes in treatment methods for patients with hepatolithiasis and investigated the most appropriate treatments for each disease type. All data are expressed as mean ± SD. Statistical analysis was performed with the χ² test and t test. Probability differences of .05 or less were considered significant.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hepatolithiasis</th>
<th>Cholecystolithiasis</th>
<th>Choledocholithiasis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>56 ± 10.9†</td>
<td>50.5 ± 14.5</td>
<td>64.4 ± 13.9</td>
<td>54.8 ± 15.2</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>43/46</td>
<td>793/942</td>
<td>185/195</td>
<td>1021/1083</td>
</tr>
<tr>
<td>History of biliary surgery, yes/no‡</td>
<td>68/21</td>
<td>306/1329</td>
<td>182/118</td>
<td>536/1488</td>
</tr>
</tbody>
</table>

*P<.05 compared with cholecystolithiasis.
†P<.01 compared with cholecystolithiasis and choledocholithiasis.
‡P<.01 compared with cholecystolithiasis and choledocholithiasis.

and recurrent stones occur in 20% of treated patients. To decrease residual and recurrence rates, it will be necessary to accurately diagnose the complex pathologic features of hepatolithiasis and select the most effective treatment for each type of hepatolithiasis. In the present study, we clarify the indication of invasive and noninvasive treatments and procedures for patients with hepatolithiasis. Patients with hepatolithiasis were older (mean age, 56.9 years) than patients with cholecystolithiasis (P<.001), but were younger than those with choledocholithiasis (P<.001). There were no differences among the 3 disease entities in terms of age or sex (Table 1). Comparing data from 1971 through 1985 with those from 1986 through 2000, the number of patients with cholecystolithiasis increased, whereas there was no change observed in the number of those with choledocholithiasis and hepatolithiasis (P<.05).

There were chronological changes in the prevalence of various hepatolithiasis types. The L or R type comprised 17 cases (13 L type and 4 R type), whereas the LR type comprised 25 cases in 1971 through 1985; however, in 1986 through 2000, the L or R type increased to 32 cases (22 L type and 10 R type) and the LR type decreased to 15 (P = .009). When hepatolithiasis was classified according to IE typing, IE type accounted for 30 cases (71%) in 1971 through 1985 and 26 cases (55%) in 1986 through 2000, and I type accounted for 12 cases in 1971 through 1985 and 21 cases in 1986 through 2000. When hepatolithiasis was classified according to LR typing, the patients with LR type hepatolithiasis accounted for 25 cases (60%) in the first 15-year period, but this decreased to 15 cases (32%) in the second 15-year period (P<.01).
There were chronological changes in treatment procedures for hepatolithiasis (Table 2). Before 1985, cholangioenterostomy (cholangiojejunostomy or cholangio-duodenostomy) was performed more frequently than hepatectomy (9 vs 25); after 1986, hepatectomy was performed more frequently than cholangioenterostomy (236±146 minutes) or T-tube insertion (186±90 minutes). The intraoperative blood loss for hepatectomy was greater than for cholangioenterostomy or PTCSL was performed more frequently than cholangioenterostomy (cholangiojejunostomy or cholangio-duodenostomy) with an incidence of residual stones of 0% vs 50%, P<.001. However, after 1986, noninvasive treatments such as PTCSL have been performed more often (7 cases). In the past, PTCSL was performed using mechanical or electrohydraulic forces or pulsed dye laser, but after 1999, PTCSL has been performed using Ho:YAG lasers (3 cases). Consequently, the rate of residual stones decreased to 0 after PTCSL procedures.

Table 3 gives a breakdown of treatments for the 3 different LR types. Hepatectomy was performed more frequently on patients with L type hepatolithiasis than other types (29 vs 5). Hepatectomy was performed on patients with R or LR type hepatolithiasis when the absence of residual stones was ensured by such a procedure. Cholangioenterostomy or PTCSL was performed more frequently for R or LR type hepatolithiasis than L type hepatolithiasis (40 vs 4). Thus, the incidence of residual stones was lower in the L type than in the LR type (0.03% vs 42.5%, P=.001) or in the R type (0.03% vs 28.6%, P=.02).

All lateral segmentectomies (n=18) were performed on patients with L type hepatolithiasis, and left lobectomy was performed on those with L (10 patients) or LR (3 patients) type hepatolithiasis. Right lobectomy (n=2) was performed on patients with R type hepatolithiasis. In addition, an extended left lobectomy was performed on 1 patient with L type hepatolithiasis.

There were no surgical deaths among the 89 patients. The surgical procedure duration was longer for hepatectomy (256±102 minutes) than for cholangioenterostomy (236±146 minutes) or T-tube insertion (186±90 minutes). The intraoperative blood loss for hepatectomy (962±364 mL) was greater than for cholangioenterostomy (542±182 mL) or T-tube insertion (486±144 mL, P<.001), whereas the durations of hospitalization were similar for hepatectomy (29±22 days), cholangioenterostomy (38±28 days), and T-tube insertion (36±30 days). Table 4 gives the type and incidence of postoperative complications. Common complications included disturbance of liver function (n=10), bile leakage (n=7), and wound infection (n=7). There were no deaths after surgery. Moreover, the incidence of mortality was similar among these groups.

The biggest advantage associated with performing hepatectomy to treat hepatolithiasis is that all hepatic stones can be removed together with the pathologic bile ducts (including carcinomatous bile ducts), thus reducing the risk of recurrent intrahepatic stones. Hepatectomy is most often indicated for the treatment of L type hepatolithiasis, and lateral segment resection or left lobe resection is performed to remove intrahepatic stones and pathologic bile ducts. The incidence of I and L type hepatolithiasis is increasing in Japan, and hepatectomy now accounts for more than half of the surgical treatments performed for I and L type hepatolithiasis.

The indications for hepatectomy are as follows: (1) hepatolithiasis is localized in the unilateral lobe, (2) the hepatic bile duct containing stones is markedly constricted or dilated, (3) combination with intrahepatic bile duct carcinoma, or (4) hepatolithiasis is accompanied by hepatic lesions including hepatic abscess or atrophy. Thus, hepatectomy is usually performed on patients with L type hepatolithiasis and rarely on patients with R type hepatolithiasis. Our data showed that left hepatic resection was performed more frequently than right hepatic lobectomy (32 vs 3).

When hepatectomy is not indicated, cholecdochojejunostomy is often performed to treat hepatolithiasis. There

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Table 2. Treatment Procedures for Hepatolithiasis*

<table>
<thead>
<tr>
<th>Years</th>
<th>Hepatectomy</th>
<th>Cholangioenterostomy</th>
<th>T Tube</th>
<th>PTCSL†</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1971-1985</td>
<td>25 (14)</td>
<td>8 (3)</td>
<td>0 (0)</td>
<td>42 (17)†</td>
<td></td>
</tr>
<tr>
<td>1986-2000</td>
<td>12 (18)</td>
<td>4 (0)</td>
<td>7 (1)</td>
<td>47 (5)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>34 (0)‡</td>
<td>36 (18)</td>
<td>12 (3)</td>
<td>7 (1)</td>
<td>89 (22)</td>
</tr>
</tbody>
</table>

*Data in parentheses indicate the number of patients with residual stones. PTCSL indicates percutaneous transhepatic cholangioscopic lithotripsy.

†P<.05 compared with residual stones in 1986 through 2000.
‡P<.05 compared with cholangioenterostomy.

Table 3. Treatment for Hepatolithiasis According to the Location of Stones*

<table>
<thead>
<tr>
<th>Stone Location</th>
<th>Treatment</th>
<th>L</th>
<th>LR</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatectomy</td>
<td>n = 34</td>
<td>29 (0)</td>
<td>3 (0)</td>
<td>2 (0)</td>
</tr>
<tr>
<td>Cholangioenterostomy</td>
<td>n = 36</td>
<td>4 (1)</td>
<td>25 (14)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>T-tube drainage</td>
<td>n = 12</td>
<td>2 (0)</td>
<td>7 (2)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>PTCSL</td>
<td>n = 7</td>
<td>0 (0)</td>
<td>6 (1)</td>
<td>1 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>35 (11)‡</td>
<td>41 (17)†</td>
<td>14 (4)</td>
<td></td>
</tr>
</tbody>
</table>

*Data in parentheses indicate the number of patients with residual stones. L indicates left intrahepatic duct; LR, bilateral intrahepatic duct; R, right intrahepatic duct; and PTCSL, percutaneous transhepatic cholangioscopic lithotripsy.

†P<.01 compared with LR and R types of residual stones.

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are 2 problems with choledochojjunostomy. First, choledochojjunostomy is indicated when the bile duct below the hepatic portal is constricted, but contraindicated when the intrahepatic bile duct is constricted. Intrahepatic bile duct constriction could lead to severe postoperative intrahepatic cholangitis, and careful postoperative care is needed. Second, choledochojjunostomy is indicated when intrahepatic stones are seen in both lobes and residual stones are expected to remain even though extensive lithotripsy has been performed. To facilitate postoperative natural stone elimination, the T tube is placed in the common bile duct, or a retrograde transhepatic biliary drainage tube is inserted into an area of the bile duct where residual stones are found.

Therapeutic planning for hepatolithiasis begins with accurate diagnosis. An attempt should be made to perform PTCSL before other procedures to ascertain the condition of the intrahepatic biliary tract, the location of stones, and the location and severity of biliary stricture or dilatation. One of the reasons that multiple surgical procedures for hepatolithiasis are often performed is that the initial treatment is not appropriate, thus further complicating the condition due to residual or recurrent stones. In addition, PTCSL is performed for patients with intractable hepatolithiasis (ie, LR or R types where hepatectomy is not indicated).

Residual stones are the most troublesome problem after treatment for hepatolithiasis. The incidence of residual stones has markedly decreased from 19.8% to 62.3% without cholangioscopy to 10.0% to 30.2% with intraoperative and postoperative cholangioscopy. In our study, the residual stone rate after PTCSL for hepatolithiasis was 14.3%. Cholangiojejunostomy was one of the major treatment procedures for hepatolithiasis before 1985, but the rate of residual stones was 56% (14/25) after this treatment. However, after 1986, hepatectomy and noninvasive treatments, including PTCSL, have been performed with greater frequency, and the rate of residual stones has decreased to 31% (1/32) after these treatments. Lee et al reported only a 4.2% recurrent stone rate after hepatectomy. Jan et al reported that recurrent stone rates after complete stone clearance for hepatolithiasis by hepatectomy and PTCSL were 9.5% and 36.4%.

In another report of 19 patients who underwent complete lithotomy, calculi recurred in 4 (21%), 3 of which had disease recurrence less than 1 year after PTCSL. The rate of recurrent stones has been high after PTCSL, and the reason is that even when initial therapy is successful in completely eliminating stones, the structure of the bile duct remains unchanged.

In the past, lithotripsy was performed mechanically or electrohydraulically using basket forceps. In recent years, favorable results have been obtained using lasers. At our institution, we have recently used the Ho:YAG laser in 3 cases, which has been used with increasing frequency in the field of urology in recent years. To our knowledge, there have not been any previous reports on the use of Ho:YAG lasers for the treatment of hepatolithiasis. The Ho:YAG laser fragments the components and achieves high stone-free success rates clinically. Extracorporeal shock wave lithotripsy is a noninvasive treatment technique for patients. The decision whether to perform ESWL is based on the type of stone and is indicated for the treatment of cholesterol stones. Also, stones can become trapped in the common bile duct during ESWL for hepatolithiasis, leading to severe acute suppurative cholangitis. Therefore, it is necessary to perform drainage procedures such as PTCD beforehand. Because 4% to 7% of patients with hepatolithiasis have intrahepatic bile duct carcinoma, it is necessary when performing PTCS or ESWL to perform a bile duct biopsy to ascertain the hardness and color of the bile duct wall and determine whether dilation or constriction of the bile duct has resulted from inflammation or cancer. These findings suggest that cholangiojejunostomy or T-tube drainage is sufficient for the treatment of stacked intrahepatic stones secondary to choledocholiths when unaccompanied by hepatic atrophy or intrahepatic bile duct constriction. However, in the case of primary hepatolithiasis, ESWL should be performed first for cholesterol stones, hepatectomy should be performed first for L and R type bilirubin calcium stones, and PTCSL should be performed first for LR type and recurrent stones. In the case of secondary hepatolithiasis (following choledocholithiasis), if there is no liver atrophy and no stenosis of intrahepatic duct, cholangioenterostomy, T-tube drainage.

Table 4. Morbidity and Mortality After Surgery for Hepatolithiasis

<table>
<thead>
<tr>
<th>Complication</th>
<th>Hepatectomy (n = 34)</th>
<th>Cholangioenterostomy (n = 36)</th>
<th>T-Tube Drainage (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with complications, No. (%)</td>
<td>8 (24)</td>
<td>9 (25)</td>
<td>5 (38)</td>
</tr>
</tbody>
</table>

*Other complications included intra-abdominal bleeding in the heptatectomy group, acute gastric mucosal lesion in the cholangioenterostomy group, and acute pancreatitis in the T-tube drainage group.
Decision tree for treatment of hepatolithiasis. In the case of primary hepatolithiasis, extracorporeal shock wave lithotripsy (ESWL) should be performed first for cholesterol stones, hepatectomy should be performed first for bilirubin calcium stones located in the left (L type) or right (R type) intrahepatic duct, and percutaneous transhelical cholangioscopic lithotripsy (PTCSL) should be performed first for stones located in the bilateral intrahepatic duct (LR type) and recurrent stones. In the case of secondary hepatolithiasis (following choledocholithiasis), if there is no liver atrophy and no stenosis of intrahepatic duct, cholangioenterostomy, T-tube drainage, or endoscopic sphincterotomy should be performed.

Hepatectomy

ESWL

PTCSL

L

R

LR

Cholangioenterostomy

T-Tube Drainage

EST

ESWL

Primary Intrahepatic Stones

Secondary Intrahepatic Stones (Following Choledocholithiasis)

Cholesterol Stones

Bilirubin Calcium Stones

Recurrent Stones

(No Liver Atrophy, No Stenosis of Intrahepatic Duct)

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References


In Other AMA Journals

Archives of Internal Medicine

An Update on Hypercoagulable Disorders

Daniel G. Federman, MD; Robert S. Kirsner, MD

Venous thrombosis is a cause of considerable morbidity and is often responsible for chronic venous disorders that frequently lead to visits to dermatologists and others involved in wound healing. Over the past several years, many new causes of thrombophilia have been identified and have dramatically altered the approach to patients presenting with thrombosis. Newly described abnormalities associated with thrombophilia include the syndrome of activated protein C resistance, the prothrombin 20210A mutation, hyperhomocysteinemia, and elevated levels of coagulation factors VIII and XI. Clinicians can now frequently determine causes of thromboses that have previously been deemed idiopathic. (2001;161:1051-1056)

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