Are Expandable Metallic Stents Better Than Conventional Methods for Treating Difficult Intrahepatic Biliary Strictures With Recurrent Hepatolithiasis?

Kuo-Shyang Jeng, MD; I-Shyan Sheen, MD; Fi-Sh Yang, MD

Background: Conventional methods for treating patients with recurrent hepatolithiasis associated with complicated intrahepatic biliary strictures include balloon dilatation of the intrahepatic biliary strictures, lithotripsy, and the clearance of difficult stones as completely as possible, with the placement of an external-internal stent for at least 6 months. After these modalities are used, symptomatic refractory strictures remain. Recently we used internal Gianturco-Rosch metallic Z stents to treat patients who had refractory strictures.

Objective: To compare therapeutic results and complications of an internal expandable metallic Z stent with those of repeated external-internal stent placement.

Study Design: Case-control study.

Setting: A referral center.

Patients: From January 1992 to December 1996, 18 patients with recurrent hepatolithiasis and complicated intrahepatic biliary strictures underwent percutaneous dilatation of stricture and transhepatic percutaneous cholangioscopic lithotomy for recurrent stones. After their stones were completely cleared, their biliary strictures failed to dilate satisfactorily. The patients were randomly enrolled into 2 groups: group A (7 patients), who received an expandable metallic Z stent, and group B (11 patients), who had repeated placement of external-internal stents.

Interventions: Percutaneous stricture dilatation, electrohydraulic lithotripsy, balloon dilatation, percutaneous transhepatic cholangioscopic lithotomy, and biliary stenting by a Silastic external-internal catheter or a modified Gianturco-Rosch expandable metallic Z stent (for an internal stent).

Main Outcome Measures: The number of procedures, days in hospital, procedure-related complications, incidents of stone recurrence and recurrence of cholangitis, readmissions to the hospital, treatment sessions required, and mortality rate. Patients' limitations in ordinary activities were also compared.

Results: The follow-up period ranged from 28 to 60 (40.7 ± 12.7 [mean ± SD]) months in group A and from 28 to 49 (36.0 ± 7.2) months in group B. Fewer group A patients (3 [43%]) than group B patients (8 [73%]) tended to have recurrent cholangitis and to require readmission to the hospital, but this was not statistically significant ($P = .33$). When their cumulative probability of a first episode of cholangitis during follow-up was compared, however, it was significantly lower in patients treated with a metallic stent ($P = .04$). Compared with group B patients, group A patients had less frequent recurrence of stones (0% vs 64%; $P = .01$), fewer procedures for the clearance of biliary stones or sludge (1.7 ± 2.2 vs 6.4 ± 4.3; $P = .03$), and shorter hospital stays (8.0 ± 11.5 days vs 17.0 ± 12.0 days; $P = .07$). No patients in group A experienced limitation in ordinary activities, whereas 7 patients in group B did ($P < .02$).

Conclusions: Compared with the repeated placement of external-internal stents, the use of a metallic internal stent effectively decreases stone recurrence, simplifies further procedures, and is more convenient. Its use is suggested as an alternative choice in the treatment of recurrent hepatolithiasis with refractory intrahepatic biliary strictures.

PATIENTS AND METHODS

One hundred fifteen patients were seen with recurrent hepatolithiasis from January 1989 to December 1996. Recurrent hepatolithiasis was defined as a history of having previous surgical or biliary procedures for hepatolithiasis and no residual stones found on computed tomographic scan or endoscopic retrograde cholangiography, percutaneous transhepatic cholangiography (PTC), or T-tube cholangiography at the end of the previous treatment. Patients with an incomplete study, treatment, or follow-up were not included. Those who had cholangiocarcinoma diagnosed during the treatment or follow-up period also were excluded. Among these 115 patients, 38 patients underwent repeated surgical intervention, and 77 patients underwent PSD and PTCSL. Twenty-five patients received external-internal stenting therapy after the complete clearance of recurrent stones. They were observed at an outpatient clinic and had follow-up PTC once a month. At the end of 6 or more months, a cholangiogram showed persistent strictures in 18 patients. All these patients had evidence of cholangitis, including intermittent episodes of right upper quadrant pain (n = 18), fever (n = 18), jaundice (n = 9), and leukocytosis (n = 12). They were admitted to the hospital for treatment and entered into this study. Follow-up cholangiography through the external-internal stent showed a persistent biliary stricture without stone recurrence. External drainage of infected bile by opening the external cap of the stent and parenchymal antibiotic therapy for 1 week lessened the cholangitis. The patients were then randomly assigned to 2 treatment modalities. We planned to enroll 12 patients in each group in 5 years. At the end of 5 years, however, only 18 patients were eligible for this study.

Group A consisted of 7 patients (2 men and 5 women, ranging in age from 32-60 years) who received a modified Gianturco-Rosch expandable metallic wire Z stent (Wilson-Cook Medical Inc, Bloomington, Ind) for the internal stent. We introduced a Z stent into the intrahepatic stenotic bile duct in the following stepwise procedures. Under fluoroscopic guidance, an 8-mm balloon dilator catheter was first inserted into the dilated percutaneous bile duct (PTBD) tract. Then a 12F to 14F Teflon sheath with an introducing catheter was deployed at the long stenotic segment by withdrawing the sheath while holding the stent in position with a pusher (Figure 1). A fiberoptic cholangioscope was then inserted through the PTBD tract to evaluate the location of the stent and any migration of the stent (Figure 2). Group B patients had follow-up PTC every month to detect occlusion or migration of the stent, and the stent catheter was replaced with a new one.

The sex and age proportions and the number of previous biliary operations and previous biliary dilatation therapy, admissions to the hospital, and in-hospital days of the 2 groups were compared. During follow-up, a patient was admitted to the hospital when there was possible recurrent cholangitis (as evidenced by fever, chills, right upper abdominal pain, or jaundice) and received PTCSL to remove stones or sludge through a PTBD tract. Differentiating between calcified and soft sludge in the stenotic duct on ultrasonography and computed tomographic scan is sometimes difficult. The extracted or drained material was carefully analyzed to differentiate between stones and sludge. During re-admissions to the hospital, evidence of septicemia, bacteremia (positive results from blood cultures), or cholangitis (positive results from bile cultures) in each patient was recorded. Complications and the 1-month postprocedure mortality rate due to the entry treatments; the recurrence rate of stones, sludge, and cholangitis; the number and length of further hospital admissions; and the number of repeated biliary procedures were compared. Questionnaires about the degree of pain, the level of satisfaction, and limitations in ordinary activities were sent to both groups of patients at the end of the first 6 months of treatment. Their answers were evaluated and compared.

The Mann-Whitney U test, Student t test, Kaplan-Meier method, and log-rank test were used for statistical analyses.
current hepatolithiasis and biliary strictures.\textsuperscript{1,2} With percutaneous transhepatic manipulations, including percutaneous stricture dilatation (PSD) and subsequent percutaneous transhepatic cholangioscopic lithotomy (PTCSL),\textsuperscript{26-30} major surgical procedures are usually avoided. After balloon dilatation therapy for the strictures and repeated clearance of the stones, biliary stenting therapy is necessary for some patients with difficult strictures to maintain the ductal lumen at a minimum diameter because of the high potential for stricture recurrence.\textsuperscript{3,4} Following 6 months of stenting, a challenging problem arises when the stenotic duct fails to improve.

Self-expandable metallic stents are being used increasingly in the treatment of both benign and malignant strictures.\textsuperscript{31-41} These metallic stents capably improve our treatment of strictures in nearly all realms, such as vascular, tracheobronchial, urogenital, gastrointestinal, pancreatic, and biliary areas. In general, their use is not advisable in patients with benign conditions unless they fail to respond to other treatments. In the past 10 years, most benign biliary disorders in which metallic stents were used have been common bile (or hepatic) ductal strictures from previous operations or chronic pancreatitis. Since 1992, we have incorporated 2 options for the further treatment of these complicated cases. One is to continue using the external-internal stenting for a further 6 months. The other is to place an internal metallic stent. To our knowledge, metallic stents for benign biliary strictures in hepatolithiasis have not been applied in a large number of patients or discussed in detail.\textsuperscript{1,2,4,42} The aim of this study was to evaluate this new treatment and to compare its use with that of conventional stenting.

\section*{RESULTS}

Shortly after entry, patients in both groups were retreated successfully with stricture dilatation therapy through the PTBD tract and repeated sessions of stone extraction by PTCSL. Then either a metallic stent or an internal-external stent was placed. The procedure was successful in all 18 patients, and no 1-month fatality occurred in either group. Patients in both groups had similar baseline conditions (Table 1). The site of difficult biliary stricture was mainly on the right side because most left-sided strictures had been resected according to our strategy. One patient who had a difficult stricture at the common hepatic duct with extension to the right hepatic bile duct was entered in group A for the placement of a Z stent.
In group A, 7 patients have had Z internal stenting for 28 to 60 (40.7 ± 12.7 [mean ± SD]) months. During follow-up, 3 patients (43%) needed readmission to the hospital because of acute cholangitis (Table 2). One patient was a 58-year-old woman whose Z stent was placed between the proximal common hepatic duct and the right hepatic duct. A recurrence of cholangitis was found at the end of 6 months. She underwent the reestablishment of a PTBD. Percutaneous transhepatic cholangiography showed sludge in multiple radicles of the right intrahepatic bile ducts. Parenteral antibiotic therapy for 7 days and 4 sessions of PTCSL eradicated all the sludge. The sludge was soft, muddy, and easily removed by cholangioscopic basket catheter extraction with irrigation with an isotonic sodium chloride solution. All symptoms and signs of cholangitis subsided after treatment, she was discharged from the hospital, and has been symptom free.

A 35-year-old man with a stent in the right intrahepatic duct had been unavailable for follow-up for 12 months. Jaundice and acute cholangitis recurred 30 months after Z stent placement, and the patient was re-admitted to the hospital. We quickly reestablished his PTBD. Sludge was unexpectedly found in the lumen of the stent (Figure 3). Four sessions of PTCSL with irrigation with isotonic sodium chloride solution led to satisfactory results, and he was discharged 30 days later.

The third patient was a 57-year-old woman in whom acute cholangitis developed 7 months following Z stent placement. A PTBD was set up, and sludge without definite stones was found. The sludge was cleared after 2 sessions of PTCSL within 10 days. No migration or occlusion of stents was observed during follow-up. No clinical evidence of recurrent cholangitis or stones has been found during further follow-up.

In group B patients, who had external-internal stenting, 3 (27%) of 11 patients had stent dislodgement (Table 3). One patient experienced dislodgement of the stent 5 times in 3 months while the other 2 only had 1 dislodgement. We quickly inserted the stent into the correct position under fluoroscopic guidance. During follow-up (28-49 [36.0 ± 7.2] months), recurrent cholangitis developed in 8 patients (73%) with 14 episodes. Those incidents of cholangitis did not occur within 7 days after PTC, however. Patients with cholangitis were all admitted to the hospital and had redilatation of the PTBD tract, along with Sumitomo catheter decompression, the drainage of purulent bile, and parenteral antibiotic therapy. Stones in 7 patients and sludge in 1 patient were suspected by computed tomographic scans and PTC. These 8 patients had PTCSL, and all recurrent stones or sludge were cleared completely. Afterward, 3 patients refused to have repeated external-internal stents. All of them had recurrent cholangitis during follow-up. The other 5 patients continued with Sumitomo catheter retention for a further 6 months. The stents were then removed, and the ductal stricture abated. They have been observed in the outpatient clinic, and 3 of these 5 patients had recurrent cholangitis.

Group A patients tended to have fewer episodes of recurrent cholangitis and readmission to the hospital than group B patients, but this was not statistically significant (Table 4). When their cumulative probability of having a first episode of cholangitis during follow-up was compared, it was lower in patients treated with a metallic stent (P = .04) (Figure 4). In group A patients, stones

<table>
<thead>
<tr>
<th>Table 1. Demographic Data of Patients Receiving a Metallic Internal Stent or Repeated External-Internal Stenting*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
</tr>
<tr>
<td>Median age, y</td>
</tr>
<tr>
<td>Sex, M/F</td>
</tr>
<tr>
<td>Site of stricture</td>
</tr>
<tr>
<td>Right intrahepatic duct</td>
</tr>
<tr>
<td>Left intrahepatic duct</td>
</tr>
<tr>
<td>Common hepatic duct</td>
</tr>
<tr>
<td>History, No. (median)</td>
</tr>
<tr>
<td>Previous biliary operations</td>
</tr>
<tr>
<td>Previous biliary dilatations</td>
</tr>
<tr>
<td>Previous hospitalizations</td>
</tr>
<tr>
<td>Previous days in hospital</td>
</tr>
<tr>
<td>Patients with evidence of septicemia, bacteremia, or cholangitis, No. (%)</td>
</tr>
</tbody>
</table>

*No statistically significant difference between the groups.
recurred less frequently ($P = .01$), fewer procedures for the clearance of biliary stones or sludge were needed ($P = .03$), and the hospital stays were shorter ($P = .07$). According to the answers on the questionnaire, no group A patients experienced limitation in ordinary activities, but 7 group B patients did ($P < .02$). Of note, no cholangiocarcinoma has been found in these 18 patients.

**COMMENT**

Our results showed that cholangitis and stones recurred less frequently in patients treated with metallic stents, and they were managed more easily in at least a 2-year follow-up.

An internal stent is more convenient to use than an external-internal stent. Seven (64%) of our group B patients felt that the external-internal stent limited their working and ordinary activities for fear of dislodgement. Psychological burdens persisted until the stent was removed. Those with an internal metallic stent all returned to work and did well. In addition, various complications from the long-term use of external-internal stents, such as bile leakage; inflammation or infection of the skin around the tube; cholangitis; hemobilia; intrahepatic liver abscess; and clogging, dislodgement, or migration of the stent, are well known. A better opportunity for sludge deposition and bacterial adherence on its surface possibly results from the wall of the Yokohama stent, and its Silastic material is not as inert as the metallic material. For patients with external-internal stents, it is necessary to perform follow-up cholangiography to accurately determine the position of the internal part of the stent and to replace it with a new tube every month to prevent tube occlusion with thick bile or sludge. In contrast, no stent replacement is necessary for metallic stents, and PTC is indicated only if cholangitis recurs.

Metallic stents\textsuperscript{13-25} are composed of a thin stainless-steel wire that has been shaped into either a mesh tube (Wallstent) or zigzag bands with the ends soldered to form a cylinder (Z stent). After release from a relatively small catheter (8F-12F), they assume their final shape and achieve a large internal lumen by constant outward radial force. A skilled surgeon can place the stent easily, which minimizes discomfort and inconvenience for the patient. This Z stent has wire skirts without a true stent wall. The small surface area of the metallic stents might decrease the likelihood of bacteria adherence and other secondary depositions on its wall, which possibly decreases the risk of cholangitis. The low occlusion rate from the large lumen and low likelihood of debris deposition further decrease the risk of sepsis.

In the literature, some major (8%) postprocedural complications have been reported, such as biliary pleuritis, peritonitis, hepatic artery aneurysm, intrahepatic artery bleeding, right subphrenic abscess, and sepsis. No procedure-related deaths occurred. In our series, no pro-

---

**Table 3. Group B Patients Before and After 6 Months of External-Internal Metallic Stenting**

<table>
<thead>
<tr>
<th>Before Entry</th>
<th>Continuing External-Internal Stenting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Operations, No.</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

* Rt indicates right intrahepatic bile duct; Lt, left intrahepatic bile duct.
† The 6 months of external-internal stenting was included in the total period of follow-up.
‡ Time to the first attack of cholangitis after entry in the study.
§ Plus sign indicates present; minus sign, absent.
procedure-related complications were encountered. The long-term effects of metallic stents on the biliary wall are still unclear. Relatively mild reactive inflammatory changes observed in the wall of the bile ducts suggest that they could be used safely to relieve biliary obstruction.41 Epithelialization over the filament follows the firm anchorage of the stent to the ductal wall. Using at distal common bile duct stricture caused by chronic pancreatitis, a 90% patency rate at 3 years was observed. Only 2 incidents of occlusion occurred 1 month after the placement from excessive epithelial hyperplasia of bile duct mucosa.36 Of note, the occurrence of occlusion did not increase with longer follow-up. In patients with pyogenic cholangitis, however, Yoon et al42 reported only 62% and 27% patency rates for intrahepatic ducts and extrahepatic ducts, respectively, at 3 years. The most common causes of stent occlusion were recurrent stone or sludge and epithelial hyperplasia. They suggested that metallic stent is not an effective long-term treatment of benign biliary stricture associated with recurrent pyogenic cholangitis.

The criteria of our patients selected for metallic stents was stricter than those of Yoon et al. They all had failure of a previous dilating-stentig therapy. Four (57%) of our patients had good function of their metallic stents at 5 years, a rate that is similar to that noted by Yoon et al, and the cause of cholangitis was the presence of sludge in 2 patients and stones in 1 patient. Only 3 patients (27%) with external-internal stents had good function at 3 years, however, and the cause of cholangitis was sludge in 1 patient and stones in 7 patients. Although a metallic stent cannot keep an excellent long-term patency, the external-internal stent gave a worse result. Furthermore, it is easier to clear sludge than to clear stones.

Our series showed substantially higher stone recurrence in the group with external-internal stents, but the rate of recurrent stone and sludge did not reach a significant difference compared with that in the group with metallic stents. Interestingly, sludge was more likely to recur than stone in the group with a metallic stent, in contrast to more stone than sludge recurring in the group with external-internal stents. Biliary sludge is bile in a gel form that contains numerous crystals of calcium bilirubinate, cholesterol, and glycoproteins. Its presence implies that the nucleation of bile solute has occurred, and concrete stones may develop later.43,44 A bigger dilated lumen, inert metallic material, and the small contact surface area of a metallic stent allow a smoother and more constant flow of bile than does the Yokohama stent. So the lithogenic disease process proceeds slowly, and biliary sludge instead of stone is observed in patients with a metallic stent. Stones differ from sludge in that they are formed, harder, and more difficult to remove. The muddy sludge easily drains with bile flow after PTBD and isotonic sodium chloride irrigation with PTCSL. Similar to stones, recurrent sludge may retard bile flow and result in severe cholangitis or even septicemia. Substantially fewer percutaneous procedures were needed to treat cholangitis in group A patients than in group B patients, which supports the above observations.

Two additional points should be addressed. In the literature, 10% to 15% of patients with recurrent pyogenic cholangitis have cholangiocarcinoma. None of the patients in this study have been found to have cholangiocarcinoma. This might be due to the small number of patients and because patients with malignant lesions were excluded from the study. Group B patients had PTC every month to detect occlusion or migration of the stent, and the stent catheter was replaced with a new one. We did not consider that the cholangitis in group B was partly due to contamination of the biliary system from PTC and stent replacement because cholangitis did not occur within 1 week after the procedures. We could not definitely exclude their minor contribution to the occurrence of cholangitis, however. As to the causes of recurrent hepatolithiasis, to our knowledge, no correlation of PTC and stone formation has been found. Although PTC did not appear to be associated with more cholangitis and stone recurrence in group B patients, a decreased need for invasive procedures in group A patients (with metallic stents) is a remarkable benefit.

The firm anchorage of metallic stents to the bile duct wall and epithelialization over the mesh make stent migration almost impossible, but little chance of endoscopic removal make the use of metallic stents in patients with benign disorders debatable. Their use in refractory benign diseases, however, is increasing. Recently, Gorich et al45 reported that they successfully ex-

Table 4. Outcome of the 2 Groups After Entry in the Study*  

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group A (n=7)</th>
<th>Group B (n=11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment morbidity</td>
<td>0</td>
<td>3 (27)</td>
<td>.24</td>
</tr>
<tr>
<td>Recurrence of cholangitis</td>
<td>3 (43)</td>
<td>8 (73)</td>
<td>.33</td>
</tr>
<tr>
<td>Sludge</td>
<td>3 (43)</td>
<td>1 (9)</td>
<td>.24</td>
</tr>
<tr>
<td>Stone</td>
<td>0</td>
<td>7 (64)</td>
<td>.01</td>
</tr>
<tr>
<td>Further hospitalization</td>
<td>3 (43)</td>
<td>8 (73)</td>
<td>.33</td>
</tr>
<tr>
<td>Hospital days, mean ± SD</td>
<td>8.0 ± 11.5</td>
<td>17.0 ± 12.0</td>
<td>.07</td>
</tr>
<tr>
<td>Percutaneous procedures (sessions), mean ± SD</td>
<td>1.7 ± 2.2</td>
<td>6.4 ± 4.3</td>
<td>.03</td>
</tr>
<tr>
<td>Limitations of ordinary activity</td>
<td>0</td>
<td>7 (64)</td>
<td>.01</td>
</tr>
</tbody>
</table>

*Except where noted, data are given as number (percentage) of patients.

Figure 4. Cumulative probability of a first episode of recurrent cholangitis (P = .04)
tracted displaced metallic stents transhepatically with no complications. This challenges the previous concept of removal only by resection.

From this preliminary controlled study, the use of an expandable metallic internal stent in the management of intrahepatic biliary strictures cannot completely avoid the possibility of the recurrence of biliary sludge, stone, and cholangitis. It can effectively decrease the recurrence of cholangitis and stones, simplify further necessary treatment, and result in less limitation of ordinary activities. Therefore, its use is suggested as an alternative for the treatment of refractory recurrent hepatolithiasis with difficult strictures.

Reprints: Kuo-Shyang Jeng, MD, Department of Surgery, Mackay Memorial Hospital, No. 92, Section 2, Chung-Shan North Road, Taipei, Taiwan, Republic of China.

REFERENCES