Effectiveness of hepatic parenchyma lithotomy of hepatolithiasis:
A single-center experience

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Abstract
To investigate the clinical significance of hepatic parenchyma incision by lithotomy near the second hepatic portal area for the treatment of complex hepatolithiasis.

A retrospective study was conducted with 35 patients who had complicated hepatolithiasis in our hospital from January 2008 to December 2013, who underwent hepatic parenchyma incision by lithotomy near the second hepatic portal area. The perioperative and long-term outcomes included the stone clearance rate, operative morbidity and mortality, and the stone recurrence rate. Patients with a preoperative diagnosis of cholangiocarcinoma were excluded from the study.

All patients with hepatic duct stones were mainly located at S2, S4, and S8 regions. Surgical methods included were hepatic parenchyma incision by lithotomy near the second hepatic portal area, or by combined partial hepatectomy. The mean follow-up period was 51 months. One patient died during hospitalization. The surgical morbidity was 17.6%, stone clearance rate was 88.2%, and final clearance rate was 94.1% followed by postoperative choledochoscopic lithotripsy. The stone recurrence rate was 16.5% and the occurrence of postoperative cholangitis was 11.8% during the follow-up period.

Hepatic parenchyma incision by lithotomy near the second hepatic portal area is safe with satisfactory short and long-term outcome results for complicated hepatolithiasis.

Abbreviations: CBD = common bile duct, CT = computed tomography, ERCP = endoscopic retrograde cholangiopancreatography, ERCP = endoscopic retrograde cholangiopancreatography, EST = endoscopic sphincterotomy, ICG-R15 = 15-minute retention rate of indocyanine green, MRCP = magnetic resonance cholangiopancreatography, MRI = magnetic resonance imaging, PTCS = percutaneous transhepatic cholangioscopy, US = ultrasound.

Keywords: hepatic parenchyma, hepatolithiasis, lithotomy, second hepatic portal

1. Introduction
Hepatolithiasis is endemic in the Asia-Pacific region, where its prevalence can be as high as 30%–50%, and is also increasing more commonly with a prevalence of 0.6%–1.3% in the Western populations.[1] Hepatolithiasis is defined as the presence of gallstones in the intrahepatic bile ducts,[2] whereas complicated hepatolithiasis extends to intrahepatic strictures and bilateral stones.[3] The optimal treatment for patients with hepatolithiasis still remains unclear. In general, hepatic resection for hepatolithiasis has been considered in patients with unilateral disease.[4]

There were several difficulties associated with complicated hepatolithiasis which can affect multiple hepatic segments or patients who had undergone biliary surgery previously, and hence the treatment of this disease remains to be a challenge. In this study, we selected 35 complicated hepatolithiasis patients with hepatic duct stones which were mainly located in Couinaud segments 2, 4, and 8 (S2, S4, and S8) in our hospital, and evaluated the value of treatment for hepatic parenchyma incision by lithotomy near the second hepatic portal area.

2. Materials and methods
2.1. General information
The study included 35 patients with hepatic duct stones which were mainly located in the S2, S4, and S8 regions, and the patients who underwent hepatic parenchyma incision by lithotomy near the second hepatic portal area from January 2008 to December 2013. There were 14 men and 21 women with an average age of 53.6 years (range 34–78 years). The main symptoms of patients with hepatolithiasis included abdominal pain, fever, and jaundice. Sixteen (45.7%) patients had previously undergone one or more biliary operations, 16 (45.7%) patients also had extrahepatic stones, 3 (8.6%) patients also had liver cysts, and 2 (5.7%) had secondary biliary cirrhosis. Thirteen (37.1%) patients...
patients had history of chronic hepatitis B and 11 (31.4%) had chronic diseases, 4 (11.4%) hypertension, 2 (5.7%) coronary heart disease, and 5 (14.3%) diabetes, respectively. This study had been proved by the Second Affiliated Hospital of Nanchang University Ethics Committee.

2.2. Precise assessment of distribution of stones and liver function before operation

All patients were evaluated with preoperative ultrasound (US), contrast-enhanced computed tomography (CT), magnetic resonance imaging (MRI), or magnetic resonance cholangiopancreatography (MRCP). These examinations provided information regarding the location of the stones, and also the anatomy and lesion pathology by characterizing the patients’ biliary system. In addition to the percutaneous transhepatic cholangiography, endoscopic retrograde cholangiopancreatography (ERCP) was performed selectively for patients with intrahepatic bile duct dilatation, which aimed at delineating the site of bile duct stricture. Locations of the stones are summarized in Table 1. In all the cases with complicated hepatolithiasis, volumetric CT and 15-minute retention rate of indocyanine green (ICG-R15) were performed to estimate the volume of the liver remnant and to determine the type of surgical procedure. Patients with a pathologically confirmed benign result who were diagnosed with cholangiocarcinoma were also excluded.

2.3. Patient selection and accurate surgical planning

Surgery was performed for stones located in multiple hepatic segments which were mainly located near the second hepatic portal area, such as $S_2$, $S_3$, and $S_4$, and patients who could not tolerate to undergo the resection of all the affected hepatic segments. A detailed surgical plan was prepared based on the preoperative evaluation, and the main considerations included removal of lesions, remove all the stones, unobstructed drainage, and protection of liver function. Fiberoptic choledochoscopy and preoperative ultrasound were performed in some patients to help determine the location of bile duct stones and directly extract them with the assistance of a stone basket when needed. The treatment of the disease was performed by hepatic parenchyma incision by lithotomy near the second hepatic portal area combined with partial heptectomy and choledocholithotomy. Operative procedures are summarized in Table 2.

2.4. Surgical procedure

Surgery was performed through a right subcostal incision with midline upward extension to the xiphoid process. The incisions used for exploration of common bile duct (CBD) and hepatic ducts depended on the location of the stones. During operation, routine intraoperative flexible choledochoscopy, with or without intraoperative cholangiography, was performed. Imaging data and abdominal cavity exploration provided the location of stones, liver atrophy, and hyperplasia. Routine use of US during the operation also helped us in understanding the position and size of stones, and the conditions associated with bile duct stricture or dilatation.

Before incising the liver, we could preset hepatic blood flow occlusion belt to reduce bleeding. The hepatic calculus near the second hepatic portal area could not be removed by the surgery of common bile duct combined with choledochoscopy (Fig. 1). The treatment of hepatic parenchyma incision by lithotomy near the second hepatic portal area was an option and consideration in patients who could not tolerate the resection of multiple hepatic segments.

During the operation, we could touch the liver parenchyma with fingers to roughly explore the place of calculus in the hepatic segments. Intraoperative US was performed to locate the position of the diseased bile duct which was brought to the center, sewed with several needles on both sides, and was used as an intraoperative traction. Through the intraoperative US real-time monitoring, we could avoid the damage to the intrahepatic major blood vessels (such as hepatic right and middle veins). An antegrade incision was incised on the surface of the liver parenchyma (Fig. 2) where the calculus was located, exposed the dilated intrahepatic bile duct, and removed the stones completely from the diseased hepatic bile duct (Fig. 3A). In addition, choledochoscopy was performed again to affirm the unobstructed stones between hepatic hilar bile duct and common bile duct,

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| Hepatic segments | No. of patients (n=35) |
|------------------|------------------------|
| $S_2$, $S_3$, $S_4$ | 5 (14.3%) |
| $S_2$, $S_3$, $S_4$, extrahepatic stones | 5 (14.3%) |
| $S_2$, $S_3$, $S_4$, extrahepatic stones | 6 (17.1%) |
| $S_2$, $S_3$, $S_4$, extrahepatic stones | 4 (11.4%) |
| $S_2$, $S_3$, $S_4$, extrahepatic stones | 3 (8.6%) |
| $S_2$, $S_3$, $S_4$, $S_7$, extrahepatic stones | 2 (5.7%) |
| $S_2$, $S_3$, $S_4$, extrahepatic stones | 4 (11.4%) |
| $S_2$, $S_3$, $S_4$, extrahepatic stones | 3 (8.6%) |
| $S_3$, $S_4$, $S_5$, extrahepatic stones | 3 (8.6%) |

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Table 1. The location of stone.

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Table 2. Operative procedures.

| Procedure | No. of patients (n=35) |
|-----------|------------------------|
| Hepatic parenchyma incision by lithotomy near the second hepatic portal area | 7 (20.0%) |
| Hepatic parenchyma incision by lithotomy near the second hepatic portal area + partial heptectomy | 12 (34.3%) |
| Hepatic parenchyma incision by lithotomy near the second hepatic portal area + choledocholithotomy | 11 (31.4%) |
| Hepatic parenchyma incision by lithotomy near the second hepatic portal area + partial heptectomy + choledocholithotomy | 5 (14.3%) |
and checked whether residual stones were present to assess the immediate stone clearance rate (Fig. 3B). Then, we used the 4-0 Prolene nonabsorbable line to close the hepatic bile duct. After that, we employed the silk thread to close the full-thickness surface of liver parenchyma which was discontinuous (Fig. 4). Another hepatic lobe with severe atrophy or proximal bile duct with significant stricture during the operation should be resected. Hence, a “T” tube should be placed as external drainage after choledocholithotomy.

### 2.5. Follow-up

Liver function tests were performed in all patients on postoperative days, 1, 3, and at week 1 in the inpatient clinic, and underwent regular postoperative follow-ups every 2 to 3 months by US or CT. MRCP and ERCP were performed whenever the patients presented with symptoms suggestive of cholangitis, to investigate for any further recurrence of stones. In this study, a patient died of hepatic failure due to sudden severe hepatitis and secondary biliary cirrhosis within 1 week after surgery. At the end of the study (December 2013), 34 of 35 patients completed a median follow-up period of 51 months (12–70 months).

Short-term outcomes included stone clearance rate and operative morbidity, and the long-term outcomes included stone recurrence rate and recurrence attack of acute cholangitis.

### 2.6. Statistical analysis

Data were analyzed retrospectively. Continuous data were expressed as mean ± SD.

### 3. Results

#### 3.1. Short and long-term outcomes

The overall operative morbidity and hospital mortality rates were 17.6% and 2.9%, respectively. Stone clearance rate was 88.2% and the final clearance rate was 94.1% followed by postoperative choledochoscopic lithotripsy. Residual stones could not be completely removed in 2 patients. The most common complications were bile leakage, followed by intra-abdominal abscess and wound infection.

At the end of this study, 34 patients had completed the follow-up, were completely removed at initial operation in 32 patients,
and 2 patients were retained with residual stones. With a median follow-up of 51 months, of the 32 patients who had no residual stones, 5 (15.6%) patients developed recurrent stones. Four patients suffered from at least 1 attack of acute cholangitis. The occurrence of acute cholangitis was 11.8% (4/32). Stone recurrence and residual stones were the major causes of postoperative acute cholangitis. The details of these patients are shown in Table 3.

4. Discussion

The morbidity of hepatolithiasis is associated with repeated cholangitis, which can lead to progressive biliary strictures, abscess, cirrhosis, atrophy of the affected liver, and even cholangiocarcinoma. Treatment requirements in hepatolithiasis may vary and may involve a multidisciplinary approach. Nonoperative treatments offer attractive alternatives, particularly for patients with mild extensive form of hepatolithiasis, for older patients with prohibitive operative risk, and for those with multiple previous operations. Surgery remains the main treatment option for hepatolithiasis with the main aim to completely remove the stones, remedy for strictures, free drainage, prevent recurrent hepatolithiasis, restore the biliary tract to normal physiological function, and cure disease.

In most cases of hepatolithiasis, atrophy and/or anatomical changes existed in the hepatic parenchyma, and intraoperative bleeding was increased when the lesions with hepatic atrophy were resected. In fact, hepatic resection for hepatolithiasis has been considered as the treatment of option in patients with unilateral disease; however, difficulty remains when patients present with bilateral disease.

With improved diagnostic modalities, accuracy in diagnosing hepatolithiasis has been increased. Some authors adopted anatomic liver resection as an effective treatment strategy in patients with hepatolithiasis and was associated with low morbidity and no mortality rates. Recent advances in surgical techniques and perioperative management have expanded the indications of hepatectomy in patients with hepatolithiasis, allowing those patients at high-risk to undergo hepatectomy. But it is difficult to treat and manage complicated hepatolithiasis.

Recently, few authors have reported that partial hepatectomy along with choledochoscopy for patients with bilateral hepatolithiasis were considered to be safe and efficacious treatment. Bilateral hepatectomy for the affected segments was feasible, but under a prerequisite of sufficient liver remnants. Chen et al. showed that hepaticocutaneous jejunostomy was useful for the removal of residual stones or recurrent stones, and was particularly indicated in patients with residual stone disease after hepatic resection on 1 side. The optimal management of patients with bilateral hepatolithiasis remains to be a difficult and challenging task. There have been limited data that address the management of bilateral hepatolithiasis.

To the best of our knowledge, our series is the first to report regarding the hepatic parenchyma incision by lithotomy near the second hepatic portal area for the treatment of complicated hepatolithiasis or bilateral hepatolithiasis. Compared with other studies, patients in our study had special characteristics, which included the following:

1. Patients’ stones were mainly located near the second hepatic portal area (S2, S4, and S8), but the affected bile duct showed no severe stricture.
2. Majority of our patients lived in the poor rural areas which is less accessible to good medical facilities. These patients usually presented with a more advanced stage of the disease. Some patients had a history of hepatitis, cardiovascular disease, or biliary tract surgery.
3. Owing to the long-term recurrent cholangitis and obstructive jaundice, our patients were often accompanied by varying degrees of cholestatic liver function damage and secondary biliary cirrhosis.

Multiple hepatic segments of hepatolithiasis showed atrophy and the liver parenchyma around the lesion were hypertrophied, and hence anatomical changes existed in the hepatic parenchyma. Liver function was under a critical state as most liver functions relied on the hypertrophied liver segments. So, bilateral hepatectomy for complicated hepatolithiasis demonstrated difficulty in the maintenance of liver function by the remnant liver. We also did not perform hepaticojejunostomy for it because hepaticojejunostomy cannot drain residual stones effectively in this condition, and involves a high incidence of cholangitis after surgery. Surgery for complicated hepatolithiasis was different from that of liver cancer, as we should consider the number and position of intrahepatic bile duct stones, whether there are biliary strictures and fibrotic or atrophic liver parenchyma in complicated hepatolithiasis. Furthermore, patients with hepatolithiasis had uneven liver texture; sometimes even a small part of the liver resection may cause a great damage to the liver function, and even lead to liver failure and death.

Finally, by summarizing the operation skills of hepatic portal superior approach hepatectomy and the locations of intrahepatic stones within the segments, we found that the hepatic parenchyma incision by lithotomy near the second hepatic portal area could be a better surgical method.

Hepatic parenchyma incision by lithotomy near the second hepatic portal area is based on a preoperative and intraoperative location of the calculi in the intrahepatic bile ducts. The path of operation bypasses the complicated anatomy of the first hepatic portal area. According to the intrahepatic bile ducts diseased range, condition of liver surface, and the principle of “damage control,” we could keep enough residual liver volume, remove stones completely, and reduce the postoperative complications and surgical risks. Our results demonstrated that stone clearance rate after surgery was 88.2% and final clearance rate was 94.1% followed by postoperative choledochoscopy lithotripsy. The stone recurrence rate was 15.6% and the occurrence of postoperative cholangitis was 11.8%, after a median follow-up period of 51 months. Our results were similar with most of the studies that reported after hepatic resection or bilateral resection.

This indicated that hepatic parenchyma incision by lithotomy near the second hepatic portal area for complicated hepatolithiasis was safe, and its short and long-term outcomes were satisfactory.

| Variable                                      | No. of patients (n = 34) |
|-----------------------------------------------|--------------------------|
| Initial clearance rate                        | 30 (88.2%)               |
| Final clearance rate after postoperative ERCP, EST, and PTCS | 32 (94.1%)               |
| Recurrent stone                               | 5 (15.6%)                |
| Recurrence attack of acute cholangitis        | 4 (11.8%)                |

ERCP = endoscopic retrograde cholangiopancreatography, EST = endoscopic sphincterotomy, PTCS = percutaneous transhepatic cholangioscopy.

Initial clearance is defined as the clearance of stone at immediate postoperative status.

Final clearance is defined as the clearance of stone at discharge.
There are a number of postoperative complications associated with hepatolithiasis after treatment, such as recurrent cholangitis, liver abscess, secondary biliary cirrhosis, and cholangiocarcinoma. The present study shows the presence of bile duct stricture which was the strongest predictor of subsequent complications after initial treatment for hepatolithiasis. \(^{[16]}\) When the estimated future liver remnant ratio was sufficient, partial hepatectomy was performed to remove the affected liver segment with fibrotic and scarred together with biliary severe strictures in our patients. The present study shows the presence of bile duct stricture which was the strongest predictor of subsequent complications after initial treatment for hepatolithiasis. \(^{[17]}\) We have adopted this method for 2 patients, 1 of whom had no recurrence of stones.

In this study, the most common complication was bile leakage (8.8%), followed by intra-abdominal abscess (5.9%) and wound infection (2.9%). Bile leakage is defined as bile fluid draining from the peritoneal cavity or oozing from the wound, which was demonstrated by cholangiography through a T tube or transanastomotic tube. \(^{[18]}\) The factors of bile leakage are mainly due to intraoperative suture that is imprecise and inaccuracy, and its branches in the segments, so as to shorten the operation time and reduce the risk of surgery.

Through operating the hepatic parenchyma incision by lithotomy near the second hepatic portal area, following experiences were observed:

1. Complicated hepatolithiasis affects multiple hepatic segments, shows atrophy and the liver parenchyma around the lesion appears to be hypertrophied, and the surgeon should pay attention to the anatomical changes that existed in the hepatic parenchyma. Meanwhile, patients with complex intrahepatic biliary ducts always have a history of biliary tract surgery, the anatomy of hepatic portal area is relatively difficult, and the operative procedure can easily damage the hepatic pedicle's blood vessels. The advantage include avoidance of the first hepatic portal's anatomy, expose and cut open hepatic lobes and segments, better outcomes of bile duct and its stenosis, and cannot easily damage the portal vein, hepatic artery’s trunk, and its branches in the segments, so as to shorten the operation time and reduce the risk of surgery.

2. The surgeon should properly manage the affected bile duct during the operation of the hepatic parenchyma incision by lithotomy near the second hepatic portal area. It is significantly important that the surgeon should be very familiar with the location of the hepatic veins in each liver segment and the relationship with the vena cava. Hepatolithiasis disease range appears with strict segmental distribution along with the affected biliary tree; so, using the B-ultrasound examination during the surgery can fully expose the liver lobe ducts with stones which must be sliced open and then the surgeon can remove the stones completely with cholecadchoscopy. To achieve the strictured part which can be connected with grade 1 or 2 liver ducts in the hepatic portal area, we sometimes apply the balloon catheter to expand the strictured bile duct. Severe stricturing of the unresectable bile duct should be used to shape the appropriate to relieve the intrahepatic bile duct stricture. When incising the intrahepatic diseased bile duct, surgeon should employ small incision as far as possible and avoid the use of electrotome to reduce the heat damage of bile duct. The bile duct wall should be sutured continuously and delicately, the whole layer suture of bile duct wall should not be too deep because it may close the rear wall of the bile duct together with the front wall, resulting in the postoperative bile duct stenosis, and even cause massive hemobilia. Apart from this, continuous suture can reduce the residual threads in the lumen of bile duct and the risk of stone recurrence. Finally, we should place the 2 negative pressure drainage tubes under the diaphragm for the need of fully postoperative effusion or bile drainage.

3. For the hepatic parenchyma incision by lithotomy near the second hepatic portal area, we should grasp the operation time cautiously, preoperatively taking full control of cholangitis, and improve the liver function. In this study, 1 patient died of hepatic failure due to sudden and severe hepatitis and secondary biliary cirrhosis. In view of this, for patients with a history of hepatitis, we should implement the antiviral treatment as soon as possible to reduce damage to the liver function. The near the second hepatic portal area to the hepatic parenchyma incision by lithotomy can remove stones completely, save enough residual liver, obtain obvious operation effect, and lower the level of risk. But, due to the fact that liver has been in the pathological state of repeated inflammation and hyperplasia atrophy over a long period of time, it need higher requirements for the surgeon.

However, the study involved a relatively small number of patients, and it was performed at a single medical center, and thus, our results may not be the representative of the general population. Ideal surgical treatment not only relieves stricture and remove stones completely, but also needs to retain liver function as much as possible. Therefore, we should pay full attention to the preoperative assessment of liver function and the stone localization diagnosis. Evaluating patients' surgical tolerance strictly and comprehensively before operation and fully understanding the pathological conditions of the whole biliary system is required. The above data can provide reliable reference to choose a proper surgical method.

In summary, as for the treatment of complex hepatic bile duct stones, we should emphasize on the individual differences. According to our algorithm for management of complicated hepatolithiasis, the hepatic parenchyma incision by lithotomy near the second hepatic portal area was a definitive treatment. This is used to treat patients whose stones were mainly located in the segments (S2, S4, and S8), accompanied by partial liver compensatory hypertrophy around the lesions and those patients who cannot tolerate multiple hepatic segment resection.

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