



## Evolution of surgical treatment of intrahepatic lithiasis in China

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Cholelithiasis in China has undergone marked changes in its character since the 50 s, when the main features associated with biliary disease were recognized as biliary stones, infection, and parasitic infestation. However, at that time, cases of cholelithiasis accounted for only 40%-60% of the cases of biliary surgery, and 50% of them were associated with primary bile duct stones. This condition remained unchanged until the early 80 s. The Biliary Surgical Society of the Chinese Association of Surgery conducted a nationwide survey of 11342 surgical cases of cholelithiasis enrolled from 146 hospitals between 1983 and 1985. This survey revealed that the relative incidence was 52.8% for cholecystolithiasis, 11.0% for secondary common bile duct stones, 16.1% for intrahepatic duct stones, and 20.1% for extrahepatic bile duct stones. Thus, the relative incidence of primary bile duct stones (36.2%) had decreased. Ten years later, the survey was repeated in 1992, and the results showed a tendency of drastic decrease in the occurrence of bile duct stones, evidenced by the decrease to 5% in the relative incidence of intrahepatic bile duct stones.

However, intrahepatic bile duct stones are not completely eliminated in our country and in the Far East. A comparative survey by Nakayama (1986) revealed that the relative incidence of intrahepatic bile duct stone was 4.1% in Japan, while the relative

incidence of hepatic bile duct stone in Taiwan is reported to be the highest in the world (53.3%). However, in a retrospective review of cases of cholelithiasis from 28 hospitals in Taiwan during a 20-year period (1971-1990), Su *et al* found that intrahepatic bile duct stones accounted for 20.3% of 17182 surgical patients of cholelithiasis. This indicates that the incidence of intrahepatic lithiasis is slightly higher than that in the mainland of China.

Regional differences in the prevalence of intrahepatic bile duct stones in our country are remarkable. The incidence of intrahepatic bile duct stone among autopsy and clinical cases of cholelithiasis was 38% and 24.6%, respectively, in Chongqing; 18.7% and 31% in Chengdu and Luzhou, respectively; 43.1% in Shantou; and only 4.5% in Shanghai. It was low in the northwest and north of China (4.8% and 4.1%, respectively). A general tendency of decrease in the relative incidence of intrahepatic bile duct stones and reduction in the number of new patients diagnosed was noted. However, this change was not paralleled in different areas of the country; for example, in a 10-year survey (1981-1991) conducted in Guangxi Province, the relative incidence of gallbladder stones rose from 12.7% to 19.8% in the latter 5 years, while the incidence of bile duct stone decreased only from 55.2% to 41.8% during the same period. Therefore, intrahepatic bile duct stone was still a common disease that remains difficult to treat in many inland provinces, where the disease is not only disappearing, but also attracted more attention than before.

The basic principles of surgical treatment for intrahepatic bile duct stones are relief of obstruction, elimination of lesion, and adequate drainage. The key aspect of surgical treatment is "elimination of lesion". Intrahepatic bile duct stone is a condition with strictly intrahepatic segmental distribution; corresponding pathological changes have been reported to occur in different areas of the liver, *e.g.*, fibrosis, atrophy, and dysfunction. Huang ZQ (1957) advocated the use of planned hepatic lobectomy for treating intrahepatic bile duct stones and reported one case of left lateral hepatic lobectomy and another case of right hepatic lobectomy. Hepatic lobectomy has been gradually and widely been accepted as the treatment for intrahepatic bile duct stones, and it is now a common procedure for treating gallstones in the left lateral lobe of the liver. In a national survey on surgical therapy for intrahepatic bile duct stones occurring in 4197 patients, hepatic lobectomy was used for the treatment of 728 cases (17.3%). According to a recent report, hepatectomy rates ranged from 11% to 32% in 4 groups of surgical patients with hepatic bile duct stones, with the mean rate being 18%. The percentage of hepatectomy among the surgical procedures performed in cases of intrahepatic stones were 49.8% and 56.6% in two core hepatobiliary centers in the mainland and about 50% in Taiwan. However, as for the location of hepatectomy, 85% of the cases were of lateral left lobectomy and 95% were of left hepatic lobectomy, 10% and 17% were of right hepatic lobectomy in some hepatobiliary centers. A discrepancy was noted in the number of cases of right-sided hepatectomy between the location of hepatectomy and distribution of gallstones. Patients with intrahepatic bile duct stones often had serious

**Table 1** The surgical therapeutic outcomes for intrahepatic bile duct stones (1963~1975)

| Surgery               | n   | A%   | B%   | C%   | D%   |
|-----------------------|-----|------|------|------|------|
| Hepatic lobectomy     | 43  | 58.1 | 32.6 | 9.3  | 0.0  |
| Cholangiojejunostomy  | 33  | 51.5 | 24.2 | 21.2 | 3.0  |
| Cholangioduodenostomy | 22  | 31.8 | 31.8 | 22.7 | 13.6 |
| Choledocholithotomy   | 32  | 34.4 | 21.9 | 12.5 | 31.3 |
| Total                 | 130 | 46.2 | 27.7 | 15.4 | 10.8 |

complications before hospital admission, and the operation only provided symptom relief. Therefore, the rates of infection in the biliary tract, residual gallstones, and reoperation were high. Thanks to the development and popularization of modern imaging technology, *i.e.* ultrasound and computed tomography, early diagnosis has become possible for the patients with intrahepatic bile duct stones since the 1980s. Hepatolithiasis in early phase usually presents with mild symptoms or is asymptomatic; the symptoms of infection are also mild because of the use of antibiotics. Gallstones were often limited to 1-2 hepatic segments of the liver without involvement of extrahepatic bile duct as noted in these patients. Therefore, the concept of surgical therapy for intrahepatic lithiasis should now be modified. The surgical treatment for intrahepatic bile duct stones in its early phase should be "radical" rather than targeted at achieving symptom relief. It would be reasonable if hepatic segmental or subsegmental resection were selectively performed during the early phase of the condition. Intrahepatic bile duct stones in their early phase are often restricted to the posterior segment of the right lobe and laterosuperior segment of the left lateral lobe, without gallstones in the extrahepatic bile duct.

Stricture of hepatic bile duct is an important factor influencing the operative effect of intrahepatic bile duct stones, and its incidence is sometimes high. For example, among 3938 surgical patients with intrahepatic bile duct stones in this country, 956 (24.28%) had hepatic hilar bile duct stricture; but the corresponding rates were 41.94%, 41.76% and 40.17%, respectively, in Guangdong, Hunan and Sichuan provinces. Among patients who underwent reoperation, the incidence rate of hepatic bile duct stricture was proportional with the frequency of reoperation. The main causes of failure of surgical treatment for intrahepatic bile duct stones were incomplete correction of the stricture and presence of residual stones in the liver. Thirty-four patients in a group of 130 patients who received surgical treatment for intrahepatic stones and had been followed for an average of 8 years, did not give satisfactory results; in 82% of the cases, the failure was due to the presence of uncorrected hepatic bile duct strictures.

Strictures associated with intrahepatic bile duct stones often occur in the hepatic hilum and the left hepatic duct, which appear narrow and ring-like with dilatation of the bile duct on both ends or nearly normal appearance of the bile ducts. Therefore, the narrowing of the bile duct may be corrected by proper surgery. Necessary steps for correcting the stricture for hepatic bile duct include wide incision of the stricture site to make a new posterior wall by suturing the bile duct wall and repairing the anterior bile duct wall with a Roux en Y-jejunal loop, in addition to performing extensive cholangiotomy and cholangioenterostomy. To ensure complete removal of the hepatic lesion, hepatic lobectomy was performed simultaneously during the operation; this combined operation was called "combined surgery". If the hepatic bile duct stricture could be corrected, the surgical outcomes for intrahepatic bile duct stones could be significantly improved. For example, in a series of 107 patients with intrahepatic duct stones and hepatic duct stricture followed up for an average of 4.5 years, 87.8% of the patients obtained satisfactory results; however, two patients died at the end stage of the disease, yielding a mortality rate of 2%. Among the various surgical procedures, hepatic lobectomy achieved the best results, with the success rate being 93.0%. This indicates that the outcome of the main hilar duct stricture would not interfere with that of the intrahepatic bile duct stone if the case was managed effectively. However, if hepatic duct stricture remained untreated, the prognosis would be poor. For example, in a group of 14 cases with the stricture *in situ*, 3 died, thereby indicating a mortality rate

**Table 2** The different surgical outcomes of 80 cases intrahepatic duct stones (1975~1981)

| Surgery               | n  | A%   | B%   | C%   | D%  |
|-----------------------|----|------|------|------|-----|
| Hepatic lobectomy     | 23 | 26.1 | 56.5 | 13.0 | 4.3 |
| Cholangiojejunostomy  | 43 | 27.9 | 48.8 | 18.6 | 4.6 |
| Cholangioduodenostomy | 7  | 14.3 | 57.1 | 28.6 | 0.0 |
| Choledocholithotomy   | 7  | 57.1 | 42.8 | 0.0  | 0.0 |

of 21.5%.

If intrahepatic bile duct stones can be completely eliminated in patients with mild hepatic hilar duct strictures, pediculated tissues were selectively used to repair the bile duct defect after incision of the stricture. The tissues used are gallbladder wall, serosal patch of the stomach, jejunum, or round ligament flap with blood supply. The repair yielded good outcomes in the early phase, owing to the preservation of the function of Oddi's sphincter and decrease in retrograde biliary infection; however, it is still difficult to arrive at a final conclusion because the number of the patients treated in this manner was small and the follow-up period was short.

Occasionally, intrahepatic bile duct stones may be extensively distributed in the liver, and in such cases, to gain access to all the major hepatic ducts, the hilar bile duct may need to be widely incised to remove stones under the field of vision. Investigations in autopsied liver specimens and clinical experiences indicated that it is possible to make a wide incision linking the right anterior inferior hepatic bile duct, right hepatic duct, left hepatic duct, and left medial hepatic bile duct. Through this 5-8 cm-long incision, the openings of 2-3 grade intrahepatic ducts can be directly visualized. Sometimes the resection of the quadratus lobe may also be performed to further widen the operative field of the hilar biliary tract, thus making the operation easier and more perfect.

Biliary tract carcinoma complicated with gallstones is an important concern to be considered during the surgical treatment of intrahepatic bile duct stones. According to a national survey of 826 surgical cases of extrahepatic biliary carcinoma studied between 1977 and 1989, 140 (16.9%) cases were associated with gallstone. In another report on 4197 cases of intrahepatic bile duct stones, 14 (0.68%) cases were associated with biliary carcinoma. The incidence of coexisting biliary carcinoma with intrahepatic duct stones varied between 0.36% and over 10%; this variation may be attributed to the differences in the subjects involved, methods of diagnosis, and the length of follow-up. Sanes and McCallum (1942) first reported two cases of intrahepatic bile duct stones associated with biliary carcinoma. Subsequently, Koga and Chijiwa reported an incidence of 2% and 7.3% of biliary carcinoma in intrahepatic bile duct stones in Japan, respectively. A study from Taiwan indicated an incidence of 5.0%, where peripheral cholangiocarcinoma was detected during autopsy in 10% of the patients with intrahepatic bile duct stones. Cholangiocarcinoma may be discovered during surgery performed for intrahepatic bile duct stones or may develop several years after the operation; therefore, it is called delayed hepatic duct carcinoma. We investigated 6 cases of hilar cholangiocarcinoma coexisting with intrahepatic bile duct stones, accounting for 1.46% of the surgical cases of intrahepatic duct stones. Guo Hong Guang *et al* reviewed 12 cases of delayed hepatic duct carcinoma after the surgery for primary intrahepatic duct stones between 1981 and 1994, accounting for 1.5% of the operative cases of intrahepatic duct stones during the same period. Hepatic duct carcinoma was noted 3-40 years (average, 10 years) after the first biliary operation for hepatic duct stones. All the patients had history of biliary disease spanning 10-40 years, and 8 of them showed nothing remarkable in endoscopic retrograde cholangiopancreatography (ERCP) before the diagnosis of the carcinoma was established.

If the resected liver specimens for intrahepatic stones were examined, the incidence of associated hepatic duct carcinoma could be even higher. In six recently published reports in this country encompassing 661 cases of hepatic lobectomy for removal of intrahepatic duct stones, 16 (2.4%) of the cases were of cholangiocarcinoma. Chang Hai Hospital in Shanghai and the 47<sup>th</sup> Hospital of PLA reported hepatic cancer in 3.33% and 3.36%, respectively, of their resected liver specimens, while 3 (4.7%) of

**Table 3 The surgical outcomes of intrahepatic duct stones (Cai-Jing Xiu, 1983 ~ 1994)**

| Surgery                                    | n   | A%   | B%   | C%   | D%  |
|--------------------------------------------|-----|------|------|------|-----|
| Hepatic lobectomy                          | 181 | 75.7 | 17.1 | 4.4  | 2.7 |
| Hepatic lobectomy and cholangioenterostomy | 192 | 58.3 | 33.0 | 7.3  | 2.0 |
| Cholangioenterostomy                       | 220 | 49.1 | 40.9 | 5.5  | 4.5 |
| Choledocholithotomy                        | 156 | 42.9 | 28.8 | 21.1 | 7.0 |
| Total                                      | 749 | 56.6 | 30.4 | 8.6  | 4.0 |

63 cases of liver specimens exhibiting malignant changes at Queen Mary Hospital in Hong Kong. Chronic intrahepatic duct stones, biliary infection, and cholestasis can result in atypical hyperplasia of the epithelial mucosa of the hepatic bile duct, which may occur as part of precarcinomatous changes.

Surgical treatment of intrahepatic bile duct stones have improved over the last few decades. However, current treatment options are far from achieving complete cure, and problems such as residual stones, recurrence and progressive liver damage still await solution. At present, multiple surgical procedures for intrahepatic bile duct stones are in use, but they may be broadly classified under three main categories, namely, hepatic lobectomy, cholangioenterostomy, cholangiotomy with T-tube drainage. In fact, the above methods are often used in combination. Our experiences with various surgical techniques over 40 years of clinical practice can be chronologically arranged into three stages: 1963-1975, 1975-1981, 1983-1994. Since all the practice was centralized and carried out under a stable leadership, the stages were comparable (Tables 1-3). The success

rates (A + B) of the three stages were 73.9%, 80.1% and 87.05%, respectively. Unfortunately, only half the patients became completely asymptomatic after the operation, and the frequency of symptom recurrence might increase over a prolonged follow-up period.

The relationship between the therapeutic effect and different operative methods were affected by several factors. If the liver lesion was not removed by liver resection, the outcome of choledochoduodenostomy was usually poor, with patients frequently developing serious postoperative retrograde biliary infection.

Hepatic lobectomy has the best outcomes, with a long-term success rate of 91.16% among 439 cases. The better result of hepatectomy was confirmed by many other reports from our country. Hepatic lobectomy is usually combined with cholangioenterostomy to solve cholestasis. For example, 368 (81.3%) of 482 cases of hepatic lobectomy were associated with various cholangioenterostomies at the Chongqing Southwest Hospital. However, the patients with limited intrahepatic bile duct stones who were treated only by hepatic lobectomy gave better long term outcomes than the patients by combined cholangioenterostomy.

Although hepatic lobectomy may remove lesions in the liver, it does not eliminate the possibility of recurrent stones in the remnant portion of the liver; this was shown in the study conducted at Queen Mary Hospital in Hong Kong, which showed that 16% of the 63 cases of hepatic lobectomies had recurrent gallstones in a new area of the liver after a median follow-up period of 47 mo. Thus, the continuation of treatment even after hepatic lobectomy is necessary, and further investigations on the prevention of the recurrence of gallstones are imperative.

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