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Congenital Anomaly of Low Insertion of Cystic Duct

Endoscopic Retrograde Cholangiopancreatography Findings and Clinical Significance

Jung-Ta Kao, MD,† Chung-Mou Kuo, MD,‡ Yi-Chun Chiu, MD,‡ Chi-Sin Changchien, MD,‡ and Chung-Huang Kuo, MD‡*

Background/Aim: Low insertion of cystic duct (LICD) may be problematic during cholecystectomy. This study was performed retrospectively to assess the prevalence of LICD and identify the risk factors of stone recurrence between LICD and non-LICD (NLICD) after removal of stones.

Methods: Between January 1999 and November 2005, 3546 patients received endoscopic retrograde cholangiopancreatography examination for suspicion of biliary tract diseases. The age and sex-matched group with NLICD was enrolled to compare the clinical differences with LICD group. LICD was defined as "the orifice level of the cystic duct being below the low third of the extrahepatic duct." Recurrence was defined as "patients suffering from cholangitis or biliary stones 1 year later after the first intervention."

Results: Of the enrolled 3546 patients (male/female = 1821/1725), 191 (5.4%) had LICD. Excluding cases of malignancy, nonbiliary stones, and incomplete data, 122 LICD patients were available. Periampullary diverticula and positive bacterial culture from bile were less common in the LICD group than the NLICD group ($P = 0.045$; $P < 0.001$, respectively). Lower recurrent rate of common bile duct (CBD) stones in the recurrent cases were found in the LICD group compared with the NLICD group ($P = 0.024$; $P = 0.039$, respectively). Univariate analysis revealed that LICD [odds ratio (OR) = 0.284; $P = 0.032$] and CBD stones (OR = 4.496; $P = 0.006$) were significantly correlated to stone recurrence.

Conclusions: Our study clearly demonstrated the prevalence (5.4%) of LICD in cases with suspicion of biliary tract disease based on endoscopic retrograde cholangiopancreatography. Notably, the strongest predictors, NLICD and CBD stones, appeared to result in the higher stone recurrence.

Key Words: biliary variants, low insertion of cystic duct, prevalence and recurrence, endoscopic retrograde cholangiopancreatography

(*J Clin Gastroenterol* 2011;00:000–000)

Received for publication April 19, 2010; accepted March 23, 2011.

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All the authors have seen and approved the content and have contributed significantly to the study. There is no any conflict of interest for all of the authors or any funding from institutions, organizations, or companies in this study.

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Biliary tract disease is a very common medical problem and often needs emergent intervention. In the United States, cholelithiasis affects approximately 10% of the adult population and the proportion increases with age. Approximately 35% of patients develop complications or recurrent symptoms leading to cholecystectomy.[1] Many technologies, such as cholecystectomy with exploration of the common bile duct (CBD), laparoscopic cholecystectomy, and endoscopic sphincterotomy play important roles in the management of biliary tract diseases.[2–4]

However, with the widespread use of laparoscopic cholecystectomy based on the advantages of short hospital stay and smooth convalescence, the frequency of iatrogenic trauma of bile ducts has substantially increased in recent years.[5] Therefore, demonstrating the anatomic variants of extrahepatic bile duct and cystic duct before surgical procedures may prevent injury to bile ducts.[6] Among anatomic variants of biliary tree,[3,4] low insertion of cystic duct (LICD) is a common variation.

The major purpose of this study is to assess the prevalence of LICD by endoscopic retrograde cholangiopancreatography (ERCP). The second purpose is to investigate the risk factors of stone recurrence between LICD and non-LICD (NLICD) after the primary intervention.

PATIENTS AND METHODS

Between January 1999 and November 2005, 3546 patients with suspicion of biliary tract diseases underwent ERCP examination. The examinations were performed using a standard technique and Olympus video duodenoscopes (TJF-240, Olympus, Tokyo, Japan). Sphincterotomy was performed using a standard sphincterotome or a needle knife. After cannulation, the presence of LICD was identified after contrast material injection. If stones were detected at the extrahepatic duct by cholangiography, they were extracted under fluoroscopic guidance by a basket, balloon catheter, or mechanical lithotripter.

Patients' records were checked to ascertain previous biliary tree diseases, biliary anatomy, and intervention. Cases of malignancy, nonbiliary stones, and unavailable data were excluded in this study. In addition, an age and sex-matched group with NLICD was enrolled into our study for comparing the clinical difference and recurrent rate of biliary tree stones between LICD and NLICD groups after therapeutic intervention.

Definition

LICD was defined as "the orifice level of the cystic duct being below the low third of the extrahepatic duct" (Fig. 1). Recurrence was defined as "patients suffering from

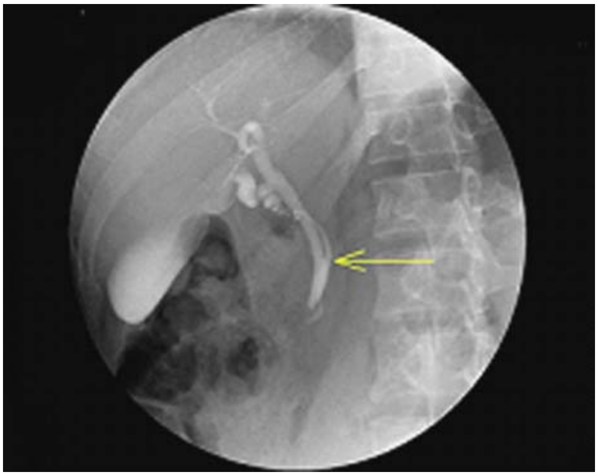

FIGURE 1. Retrograde cholangiogram demonstrates anatomic variants of the biliary tree with continuing injection of contrast; the arrow indicates low insertion of cystic duct which means orifice level of cystic duct is below the low third of extrahepatic duct.

cholangitis or biliary tree stones 1 year later after the primary intervention."

Statistical Analysis

The baseline characters and recurrent rate between patients with LICD or NLICD group were evaluated by χ^2 test and independent *t* test and logistic regression. The statistical significant difference was noted when *P* value was <0.05.

RESULTS

During the period of study, 3546 patients (male in 1821 and female in 1725) were available. The anatomic variation of LICD was detected in 191 cases (191/3546 = 5.4%) by ERCP. After excluding the cases of malignancy, nonbiliary stones, and incomplete data, 122 LICD cases (male/female = 59/63; mean age, 63.89 ± 13.23 y) with biliary stones and cholecystitis or cholangitis were enrolled into our study to compare with NLICD cases (male/female = 59/63; mean age, 64.07 ± 13.00 y) for evaluation of clinical significances.

The baseline characteristics of both LICD and NLICD groups are shown in Table 1. Of these parameters, the LICD group had significantly lower rate of periampullary diverticula and positive bacterial culture from bile than patients in the NLICD group (9.83% vs. 18.85%, *P* = 0.045; 11.48% vs. 38.52%, *P* < 0.001, respectively). Among positive bacterial culture from bile, *Escherichia coli*, *Enterococcus* sp., and *Klebsiella pneumoniae* were revealed as the predominant 3 bacteria either in the LICD (6 of 14, 5 of 14, 4 of 14, respectively) or the NLICD group (28 of 47, 23 of 47, 19 of 47, respectively). As in Table 2, a significantly lower recurrence was found in the LICD group than the NLICD group (3.28% vs. 10.66%, *P* = 0.024). The recurrent duration after initial intervention was from 13 to 63 months (mean 32.25 ± 22.32 mo) in the LICD group and from 22 to 60 months (mean 39 ± 12.81 mo) in the NLICD group. Among the recurrent cases, 1 (1 of 4; 25%) showed positive bile culture in the LICD and 7 (7 of 13; 53.8%) in the NLICD group (*P* = 0.312). In addition, the cases with recurrent stones within 1 year were 4 in the LICD and 2 in the NLICD group.

Analyzing the initial intervention, surgery (laparoscopic in 105 cases; 43%; open cholecystectomy in 65 cases; 26.6%) in the NLICD group had higher recurrent rate than by endoscopic method (12.12% vs. 4.35%, *P* = 0.276) and the same as in the LICD group (12.12% vs. 4.23%, *P* = 0.073), but did not reach significantly statistical differences. There were lower ratios of CBD stones in the initial ERCP examination and recurrent biliary tree in the LICD group compared with the NLICD group (30.3% vs. 44.3%, *P* = 0.024; 3.3% vs. 9.8%, *P* = 0.039, respectively). However, multivariable model showed no significant differences of GB, CBD, primary GB, primary CBD, and primary common hepatic duct stones between LICD and NLICD groups [OR 95% confidence interval (CI), 0.714 (0.195-2.615), *P* = 0.610; 0.446 (0.091-2.181), *P* = 0.319; 0.773 (0.166-3.593), *P* = 0.743; 1.091 (0.252-4.714), *P* = 0.907; 8.027 (0.472-136.418), *P* = 0.150, respectively] on initial ERCP. There were no significant differences in clinical manifestation in initial or recurrent biliary symptoms between NLICD and LICD groups, but pain related to the

TABLE 1. Baseline Characteristics of Patients With Low Insertion of Cystic Duct and Age-matched With Sex-matched Controls With Non-low Insertion of Cystic Duct

Variables	Low Insertion of Cystic Duct (n = 122)	Non-low Insertion of Cystic Duct (n = 122)	*P*
Periampullary diverticulum, n (%)	12 (9.83%)	23 (18.85%)	0.045*
ALT (IU/L)	124.17 ± 147.46	134.84 ± 167.29	0.636
Alk-p (IU/L)	161.64 ± 186.76	144.66 ± 128.41	0.430
T-Bil (mg/dL)	2.96 ± 3.41	3.02 ± 2.80	0.895
Amylase (IU/L)	421.08 ± 1027.45	303.35 ± 560.23	0.406
Lipase (IU/L)	3147.32 ± 9794.52	1689.06 ± 5279.55	0.298
Diabetes (yes/no)	23/99	34/88	0.096
BMI (kg/m^2)	24.83 ± 3.31	24.25 ± 4.11	0.225
Fatty liver levels†(mild/moderate/severe)	42/21/2	41/26/2	0.876
Positive Bacterial culture,‡n (%)	14 (11.48%)	47 (38.52%)	< 0.001*

On the basis of the χ^2 test and *t* test.
*A *P* value below 0.05 is considered statistically significant.
†Diagnosed by ultrasonography.
‡Positive bacterial culture accord to bile.
Alk-p indicates alkaline phosphatase; ALT, alanine aminotransferase; BMI, body mass index; n, number; T-Bil, total bilirubin.

TABLE 2. Characteristics of Recurrent Cases Between the Low Insertion of Cystic Duct and Non-low Insertion of Cystic Duct

Variables	Low Insertion of Cystic Duct	Non-low Insertion of Cystic Duct	P
No. patients (%)	4/122 (3.28%)	13/122 (10.66%)	0.024*
Age (range), y	57.25 ± 18.54 (32-75)	72.38 ± 5.62(63-81)	0.201
Sex, male/female	4 (100.0%)/0	7 (53.8%)/6 (46.2%)	0.091
Intervention methods			
Endoscopic, n/N (%)	1/51 (1.96%)	1/23 (4.35%)	0.558
Surgical, n/N (%)	3/71 (4.23%)	12/99 (12.12%)	0.073

On the basis of the χ^2 test and *t* test.
*A *P* value below 0.05 is considered statistically significant.
N indicates number of intervention; n, number of recurrent cases.

right upper quadrant of the abdomen remained obvious among these 3 symptoms either in LICD (96.7%) or NLICD (95.9%) groups (Table 3). Furthermore, among 89 patients with gallbladder (GB) stones receiving surgery, 6 were recurrent, including 3 of 38 patients with LICD and 3 of 51 patients with NLICD (7.9% vs. 5.9%, $P = 0.201$).

Univariate analysis revealed LICD (OR = 0.284; 95% CI, 0.09-0.898; $P = 0.032$) and initial stone location in CBD (OR = 4.496; 95% CI, 1.529-13.219; $P = 0.006$) showed significant predictors to stones recurrence (Table 4).

DISCUSSION

Misidentification of the cystic duct can result in postoperative complications,[5,7–9] therefore, accurate assessment of the anatomic variants of the biliary tree is extremely important before operation.[10–12] Data to document the incidences of these anatomic variants have been discussed in previous studies.[6,10–12] Among the multiple modalities, ERCP has been regarded as the gold standard tool for identifying anatomic variants of biliary tree but is rarely described.[12,13] In this study, we demonstrated the prevalent rate of LICD is 5.4% by ERCP, which is compatible with the previous studies of 3.8% to 9.0% prevalence by magnetic resonance cholangiopancreatography (MRCP).[6,11,14]

However, to date, there has been no study investigating the risk factors of biliary stone recurrence in patients with LICD and NLICD after endoscopic or surgical intervention. The possible mechanisms for stone formation may lead from bile stasis and bacterial action.[15–17] LICD also results in increasing retrograde entry, cystic duct dilation, and stone migration.[18] In contrast to the previous study,[19] our study showed that patients with LICD have significantly lower recurrent rate of biliary tree stones than patients with NLICD (3.28% vs. 10.66%, $P = 0.024$). Whether it means the stones in the GB and biliary tree would easily pass into the CBD or duodenum because the orifice level of LICD is lower than that of NLICD needs confirmation through further dynamic study. However, data from our study illustrated the possibility from no significant difference in initial ERCP ($P = 0.319$ in CBD involvement and $P = 0.907$ in primary CBD) with multivariate analysis and significantly lower ratios of CBD stone occurrence in the repeat ERCP study ($P = 0.039$; Table 3) in those patients with LICD than in those with NLICD. In addition, the factors including LICD (OR = 0.284; 95% CI, 0.09-0.898; $P = 0.032$) and initial stone location in CBD (OR = 4.496; 95% CI, 1.529-13.219; $P = 0.006$) revealed the strongest predictors to stone recurrence (Table 4).

Previous literature has discussed the notion that bile stasis and bacterial action may result in stone formation.[15–17] In our study, the significantly lower ratios of positive bacterial culture from bile and periampullary diverticula were in patients in the LICD group than in the NLICD group ($P < 0.001$; $P = 0.045$, respectively) (Table 1), but did not reach significantly statistical differences to stone recurrence ($P = 0.118$; $P = 0.076$, respectively) (Table 4). However, particularly in patients with periampullary diverticula, both these factors seemed to have weak predictors to stone recurrence (Table 4). Therefore, it means that a lower ratio of stone formation would occur and the stone would be easily passed into the duodenum in LICD group compared with NLICD group because the higher rate of periampullary diverticula in the NLICD group may interrupt the outflow of the biliary tree and is associated with higher recurrent rate.

Despite no significantly statistical difference in the therapeutic methods, our study showed surgical intervention in the LICD and NLICD groups has a higher recurrent rate than by the endoscopic method (Table 2). This is reasonable, particularly in patients with complicated biliary tree diseases in the surgical group[20,21] having higher recurrence in our study.

Similar to a previous study,[19] female individuals exhibit a higher incidence in patients with LICD in this study. In addition, there was no significant difference in biliary symptoms even in the initial or recurrent cases, but right upper quadrant pain remained the predominant symptom in our study.[22]

TABLE 3. Distribution of Biliary Tree Stones and Clinical Manifestations Between the Low Insertion of Cystic Duct and Non-low Insertion of Cystic Duct (N=244)

Variables	Low Insertion of Cystic Duct	Non-low Insertion of Cystic Duct	P
Biliary stones location			
Initial involvement			
GB involvement, n (%)	92 (75.4%)	104 (85.2%)	0.053
CBD involvement, n (%)	37 (30.3%)	54 (44.3%)	0.024*
Primary GB, n (%)	66 (54.1%)	64 (52.5%)	0.797
Primary CBD, n (%)	10 (7.2%)	11 (9.0%)	0.819
Primary CHD, n (%)	15 (12.3%)	1 (0.8%)	0.000*
Recurrent involvement			
CBD involvement, n (%)	4 (3.3%)	12 (9.8%)	0.039*
Primary CBD, n (%)	1 (0.82%)	9 (7.4%)	0.01*
Clinical manifestations			
Initial symptoms			
RUQ pain, n (%)	118 (96.7%)	117 (95.9%)	0.734
Fever and/or chills, n (%)	40 (32.8%)	30 (24.6%)	0.157
Jaundice, n (%)	33 (27.0%)	44 (36.1%)	0.130
Charcot triad, n (%)	16 (13.1%)	15 (12.3%)	0.848
Recurrent symptoms			
RUQ pain, n (%)	4 (100%)	9 (69.2%)	0.205
Fever and/or chills, n (%)	3 (75%)	5 (38.5%)	0.200
Jaundice, n (%)	3 (75%)	6 (46.2%)	0.312
Charcot triad, n (%)	2 (50%)	2 (15.4%)	0.154

On the basis of the χ^2 test.
*A *P* value below 0.05 is considered statistically significant.
CBD indicates common bile duct; CHD, common hepatic duct; GB, gallbladder; n, number of cases; RUQ, right upper quadrant.

TABLE 4. The Univariate Analysis of Recurrent Cases

Variable	OR (95% CI)	*P*
Periampullary diverticulum	2.74 (0.90-8.32)	0.076
ALT (IU/L)	0.999 (0.995-1.003)	0.536
Alk-p (IU/L)	0.998 (0.993-1.003)	0.482
T-Bil (mg/dL)	0.951 (0.793-1.141)	0.590
Amylase (IU/L)	0.999 (0.997-1.001)	0.353
Lipase (IU/L)	1.00 (0.999-1.00)	0.298
Diabetes	1.402 (0.472-4.163)	0.543
Positive bacterial culture*	2.243 (0.814-6.176)	0.118
Low insertion of cystic duct	0.284 (0.09-0.898)	0.032†
Surgical intervention	3.484 (0.776-15.639)	0.103
Initial stones location		
Primary GB	0.416 (0.146-1.189)	0.102
Primary CBD	4.496 (1.529-13.219)	0.006†
Primary CHD	1.280 (0.398-4.115)	0.679

On the basis of the χ^2 test.

*Positive bacterial culture accord to bile.

†A *P* value below 0.05 is considered statistically significant.

Alk-p indicates alkaline phosphatase; ALT, alanine aminotransferase; CI, confidence interval; CBD, common bile duct; CHD, common hepatic duct; GB, gallbladder; OR, odds ratio; T-Bil, total bilirubin.

There are certain limitations in this study. First, only 1:1 LICD with NLICD cases were enrolled into this study and would lead to selective bias, but data from Table 1 elucidated this problem from even distribution in baseline characteristics of body mass index and fatty liver level between these 2 groups. Second, we failed to demonstrate the component of biliary stones, the other anatomic variants of the biliary tree, and the association in differently detectable tools, such as MRCP. However, MRCP is not regularly performed in patients with biliary tree disease in our country. Whether these variants and survey tools also have clinical difference needs to be evaluated in the future.

Despite that, our study clearly demonstrated the prevalence rate (5.4%) of LICD in patients with clinical biliary symptoms based on ERCP. Notably, the factors of LICD and initial stone location in CBD played important roles in the recurrence of biliary tree stone. We believe these findings may be a useful reference for gastroenterologists and surgeons before management of biliary tree diseases to prevent complications of postintervention.

ACKNOWLEDGMENTS

The authors are sincerely grateful to all participants in this study. The authors also thank all the research assistants for data collection.

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