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Prospective and Controlled Study

Laparoscopic Combined Choledoscopic Cholecystolithotomy verse Laparoscopic Cholecystectomy, A Prospective and Controlled Study

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Abstract

Background and Aims: Comparison of clinical outcome of Laparoscopic Combined Choledoscopic Cholecystolithotomy(L-CCC) and Laparoscopic Cholecystectomy (LC)

Methods: A prospective and controlled study was carried out in patients with gallbladder stones, with 200 cases of LCCC and 200 cases of LC. Operative duration, postoperative inpatient days, symptoms and relapse were documented. All patients were followed-up until the end of the study.

Results: The operative time of the LCCC was longer than LC (53.56±15.22 VS 29.43±10.82 min, P<0.05). No differences were found on postoperative time and other immediate complications. Patients were followed up 5 years, average 3.8 years. In the LC group, 110 cases of diarrhea (55%) were found after resuming normal diet and 6 patients transferred to open surgery in comparing with none in the LCCC group. Postoperative patients with diarrhea have to eat low fat diet to relief the symptom. At the beginning of the study (3 mon) 4 cases (2%) of relapse and 4 cases (2%) of residual were found in the LCCC group in comparing with none in the LC group, for those with relapse, stones remain the same after chenodeoxycholic acid (CA) consumption. The cost of each group is the same.

Conclusion: LCCC group takes more time than LC group without differences on postoperative hospital stay and other clinical data. LCCC group has no diarrhea while LC group has a high percentage. LCCC has a low recurrence rate in five years and deserves further study.

Keywords: Cholecystolithotomy; Laparoscopic Cholecystectomy

Introduction

Gallstones are a common disease worldwide and occur in around 4-7% of normal population in China, and reaches 10% in Shanghai area [1], it is often complicated with acute and chronic cholecystitis, pancreatitis, and gallbladder cancer etc [2]. Treatment includes various medical disciplines, but surgical treatment is dominated by cholecystectomy, and is included in Standard of Care around the world [3]. Literatures show that high rate of dyspepsia, bile reflux gastritis and diarrhea occur after cholecystectomy [4]. From our clinical observation, many patients with cholecystectomy suffer diarrhea after normal diet consumption. The importance of gallbladder also is shown in literature that a high rate of colorectal carcinoma occurred after gallbladder removal [5]. Therefore, although gallbladder is a non-vital organ, endeavors to preserve it sees worthwhile. Until now, only sporadic cholecystolithotomy cases and follow up results were reported, and it is not widely accepted by surgeons. The aim of the present study is to compare the 5-year outcome of cholecystectomy verse cholecystolithotomy in a prospective clinical design.

Materials and Methods

General Information

Under prospective and controlled design (not randomized and blind), from September 2009 to September 2014, patients with gallbladder stone were admitted into our study. The research protocol was approved by the ethics committee of the south campus, University 6th hospital, Shanghai Jiaotong University. Informed consent was obtained from each patient. According to patient's symptom, sign, preoperative laboratory, ultrasound or CT/MRCP imaging results, LCCC enrollment criteria are as following:

1. Diagnosed as gallbladder stones, without choledochol stones, no history of upper abdominal operations, and need surgical treatment.
2. Imaging check: colorful ultrasound and show gallbladder stones, no extra hepatic bile duct stones, deformity and mass. LCCC exclusion criteria:
 1. Gallbladder dystrophy or has no lumen.
 2. Gallbladder duct stone and cannot be extracted by Chole-doscopy.
 3. Diffuse intra-wall stone.
 4. Gallbladder stone with malignancy.
 5. Combined with obesity, viral hepatitis, and viral or schistosomal cirrhosis of the liver, hemolytic anemia and other blood system disease, diabetes using hypoglycemic agents. Before operation, detailed information on the advantage and disadvantage of gallbladder removal and preservation were informed, patients themselves made free choice. General an-

esthesia with intubation of trachea was conducted for all patients. Clinical information were collected and compared on Table 1 and Table 2.

Table 1. Two groups of patients in general compare

| General information | LCCC group | LC group | P value |
|--------------------------|------------|-----------|---------|
| Age(years) | 54.3±18.8 | 50.5±20.4 | 0.503 |
| Disease duration (years) | 3.4±2.5 | 3.5±2.6 | 0.724 |
| Male/female | 12/38 | 13/37 | 0.817 |
| Single/multiple stones | 19/181 | 17/183 | 0.832 |
| Asymptomatic | 155/45 | 166/34 | 0.566 |
| BMI(Kg/m ²) | 22.3±2.6 | 21.9±2.7 | 0.821 |

Table 2. Two groups of patients in general compare.

| Lab Tests | LCCC group | LC group | P value |
|-------------------------|--------------|--------------|---------|
| WBC(10 ⁹ /L) | 6.46±1.93 | 7.12±2.05 | 0.82 |
| Hb(g/dL) | 125.62±16.36 | 128.55±20.41 | 0.93 |
| Alt(IU/L) | 26.33±15.85 | 28.26±14.23 | 0.91 |
| Ast(IU/L) | 28.5±17.3 | 29.9±10.7 | 0.88 |
| TBil (umol/L) | 1.0±0.3 | 0.9±0.2 | 0.95 |
| Albumin (g/dL) | 4.1±0.4 | 4.0±0.4 | 0.94 |
| BUN(mmol/L) | 16.9±4.3 | 17.6±5.9 | 0.91 |
| Creatine (umol/L) | 1.1±0.2 | 1.2±0.4 | 0.94 |

Surgical Procedure

Surgical instruments

Two 10mm trocars, one 5mm trocar, and one or two additional trocars were applied if operative difficulties were met. Olympus high-profile laparoscope, electronic choledoscope and stone extraction basket and biopsy forceps, and other general laparoscopic instruments.

Surgical procedure

LCCC group: General anesthesia with endotracheal intubation was established, patients were in supine position. 4 trocars were introduced as LC method. After entering the abdominal cavity, a gallbladder incision at the fundus was cut according to the size of the stone assessed by Ultrasound and MRCP. Bile inside the gallbladder was withdrawn through suction first, normal saline was used to fill the lumen slowly, repeating the above maneuver several times to make the liquid inside clear, afterwards choledochoscopy was carried out to extract the stones with baskets, forceps was not allowed to use inside the lumen to take the stone out as it may crash the stones into small pieces. 3 cm or bigger stones were squeezed out the gallbladder from the outside with instruments, as they were too big

for basket lanes. For sludge or sandy stones, suction was used to remove them. Extracted stones were put into a laparoscopic sample bag and extracted from the abdominal cavity. Tiny fragments adhered or embedded in the gall bladder mucosa were removed with forceps meticulously and bleeding from the mucosa was stopped with continuous saline irrigation. After all stones were extracted, the endoscope can enter the cystic duct and bile inflow to the lumen was observed which demonstrates a patent cystic duct and gallbladder is functional, then detailed examination on every part of the gallbladder, especially the fundus, was made to make sure no stone is left, finally 4-0 absorbable thread was used to close the gallbladder with continuing absorbable suture on mucosa and serosa. After all sutures were done, the gallbladder was squeezed to check whether leakage exists, additional sutures were done if bile leakage was found. Stones were put into the sample bag, which was extracted through 10mm hole. Drainage was placed under the gallbladder to prevent leakage and removed two days later.

LC group: 4 holes method was used, for patients with severe adhesions; additional hole was introduced [6]. LC was done through dissecting the Calot's triangle first, then removing the gallbladder from its liver bed; drainage was put routinely and removed one day later.

Adjuvant therapy

Adjuvant therapy with chenodeoxycholic acid (CA) 7 mg/kg/day was given for a fixed period of six months after the procedure. It was introduced regardless of cholesterolosis exists or not.

Follow-up method

Patients were reviewed at 3, 6, and 12 months after operative procedures and then at yearly intervals. Follow up consisted of an ultrasound examination and a clinical assessment. All patients were followed-up until the end of the study.

Ultrasound examinations

Ultrasound examinations were performed on every follow up. Details of the gallbladder contents (none, sludge or stones) and appearances of the gall bladder wall (normal, focal abnormalities or thickening) were recorded. Measuring gall bladder volumes before and after a fatty meal made a functional assessment of the gall bladder. Volume (V) was calculated using the previously described ellipsoid method

where $V = 0.52 \times \text{height} \times \text{width} \times \text{length}$. Percentage gall bladder

contraction was calculated by dividing the change in volume before and after a fatty meal by the fasting volume $\times 100\%$. Gallbladder emptying was considered satisfactory if a reduction in volume of 30% or more occurred on functional assessment, and poor or non-functional below this level.

Statistics

Statview software was used to analysis the data of the two groups on surgical time, postoperative hospital stay and postoperative changes in clinical symptoms, stone recurrence. *t* test was used in numerical data. X^2 test was used for categorical data. $P < 0.05$ was granted significant difference.

Results

LCCC group

The clinical data comparing the two groups are listed in Table 3. All patients recovered without complications, resumed low fat liquid diet consumption second day after operation, and were discharged 3-5 days later. Average hospitalization was 3.36 days. No hemorrhage inside the gallbladder, bile leakage, intra-abdominal or wound abscess was found. Follow up duration was 5 years, with 3.8 years average, no diarrhea and other postoperative symptoms. Through Ultrasound checks, residual stones were found in 4 patients (2%), all occurred in the initial 3 month of LCCC with 1-2 mm in diameter; in all cases stone disappeared after 6 month chenodeoxycholic acid (CA) consumption. 4 cases had stone relapse with around 1-2 mm single stones growing gradually, the time of relapse was 6, 12, 15 and 24 months respectively, and did not disappear after CA consumption. One patients who relapsed 24 months underwent LCCC again and now had 12 months past without recurrence. LCCC group has longer operative time, but no postoperative diarrhea.

Table 3. Outcome comparison of the two groups.

| Comparison Items | LCCC group | LC group | P value |
|----------------------------------|---------------|---------------|---------|
| Transfer to Open Surgery | 0 | 6 | 0.242 |
| Surgical duration(min) | 53.56±15.22 | 29.43±10.82 | 0.041 |
| Hospital stay | 3.4±1.6 | 3.6±1.4 | 0.546 |
| Diarrhea (cases) | 0 (0%) | 110 (55%) | 0.001 |
| Relapse (cases) | 4 (2%) | 0 (0%) | 0.623 |
| Residues (cases) | 4 (2%) | 0 (0%) | 0.575 |
| Hospitalization costs (RMB Yuan) | 13452.5±331.6 | 12160.3±253.2 | 0.751 |

LC group

110 patients (55%) have diarrhea after resuming normal diet (same diet as family members), which exacerbates after fatty food intake and must eat low-fat food to relief the symptom, fecal laboratory test confirmed steatorrhea in all patients. 6 patients were transferred to open Cholecystectomy including the following situations. One patient had common bile duct (CBD) injury found intra-operatively, and was repaired through open surgery. This patient had acute cholecystitis with several 7 mm cholesterol stones incarcerated in his cystic duct, tight adhesion existed in his Calot's triangle and CBD beneath the stones was mistakenly taken as cystic duct, after gallbladder was removed, bile outflow from the upper edge of the Calot's triangle

indicated transverse complete cut of the CBD and the following detailed examination found the segmental removal of the CBD, this patient recovered well after CBD end to end anastomosis and 6 month T-tube intubation. The other five patients all had severe adhesions around the gallbladder, especially in the calot's triangle and LC cannot be done safely.

Discussions

The advantage of LCCC

Although gallbladder is not a vital organ, it has important functions: the most important one is its participation in digestion [7]. The gallbladder concentrates 700-1000ml of hepatic bile daily from liver into 30-50 ml inside its lumen, this highly concentrated bile then can be expelled into the duodenum by the stimuli of Cholecystokinin (CCK) after fat food reaches the gastric antrum, and emulsifies the fat, which can be subsequently absorbed by enterocytes. After gallbladder was removed, fat food cannot be well emulsified and adequately absorbed, therefore steatorrhea occurred. In our study, 55 percent of patients have steatorrhea after gallbladder was removed, less than the proportion of 85% in a recent report [4]; it is probably due to less fat contained in the diet of Chinese people in comparing with that of westerners [8]. However, patients underwent gallbladder preserving cholecystolithotomy procedure do not have diarrhea, their quality of life are satisfactory in the follow-up interviews. The second, gallbladder preserving procedure spares the dissection of Calot's triangle, no bile duct injury, bleeding and open laparotomy occurred in our cases, also no gallbladder bile leakage found after operation, proving the safety of one-stage closure of the gallbladder incision. Thirdly, even though gallbladder-preserving procedure is complicated than removal, there are no significant differences on hospital stay and costs. Gallbladder preserving cholecystolithotomy procedure clears the gallbladder of stones through choledoscopy and preserves a functional organ, is a valuable option for the patients.

The difference between modern gallbladder preserving cholecystolithotomy and the past

Modern gallbladder preserving cholecystolithotomy is performed through choledoscopy, which has direct vision with 5 amplification fold of the gallbladder lumen to find small stone, baskets can be used to harvest the intact stones without breaking them into small pieces, suction can be used to clear small stone and sludge, tiny fragments adhered or embedded in the gallbladder mucosa were removed with forceps meticulously and bleeding from the mucosa was stopped with continuous saline irrigation. In the past, however, cholecystolithotomy was done blindly through directly harvesting stones with curved clamps from the gallbladder, it is more easily to break the stone and left small pieces of stones and sludge, more importantly, without the choledoscope, the surgeons were not

sure of whether gallbladder is clear of stones, stone residues and recurrences occurred postoperatively in high percentages. Even so, at the beginning of our cholecystolithotomy procedure (within 3 months), 4 cases (2%) of residue were found after patients were discharged, lack of experience under choledoscope contributes to this iatrogenic left over, these residual stones disappeared after 6 months chenodeoxycholic acid consumption. Chenodeoxycholic acid is a stone and sludge dissolution agent and effective in eradicating very small stones, generally less than 6 millimeters [9]. Stone residue no longer occurred after 3 month of cholecystolithotomy experience. In addition, our cholecystolithotomy is done through laparoscopy, different from laparotomy, which usually had a more than 10cm incision in the past.

Choledoscopic Cholecystolithotomy has low recurrence rate in our study

Previous study show that recurrence occurred mainly within 5 years after cholecystolithotomy, afterwards it turns much lower, recurrence rate within 5 years was pretty high, around 40 percent [10]. Only in a recent article by Liu JS reported that 5-year recurrence rate was 6.60% [11]. Our recurrence rate is only 2 percent, the reason contributes to this low occurrence, which is dramatically different from most other observations, is that our gallbladder-preserving group has strict exclusion criteria as previously described in this paper. First, our awareness of the systemic factors are more liable contributes to recurrences [12]. Bile is synthesized by liver, its composition change is a major factor in gallstone formation [13], for patients that has a high BMI and elevated blood cholesterol level, cholesterol excretion from the bile is also increased, risk of recurrence after cholecystolithotomy is increased and not recommended. For patients with liver disease, such as hepatitis and cirrhosis, hemolytic and other kinds of anemia, increased excretion bilirubin contributes to the stone formation [14], thus cholecystolithotomy is not recommended. Diabetic patients have to use insulin and other hypoglycemic agents for life-long time and these drugs are prone to cause cholestasis [15], cholecystolithotomy is also not recommended. Second, patients had great desire to preserve their organ and were more obedient in the follow-up checks, diet and life-style regulations, including having breakfast well to promote gallbladder empty [16], reduce cholesterol food intake, and regularly measure the concentration of blood cholesterol to regulate its level. Third, oral intake of CA for three months was prescribed for every LCCC patients as a preventive method. These measures all contribute the low recurrence rate in our gallbladder preserving cholecystolithotomy patients.

Cholecystolithotomy itself has certain indications and contra-indications

Technically, not all patients with gallbladder stones are suitable for gallbladder preserving cholecystolithotomy, which is

done only when the following situations were encountered, diagnosed as gallbladder stones without choledochol stones, without upper abdominal operations, deformity and mass, also patients have desire to preserve their organ. Also for those with the following conditions: Gallbladder is not functioning or suspected of malignancy, with diffused intra-wall stones or polyps and cannot be completely taken out by choledoscopy. For stones incarcerated in the ampulla of the gallbladder, if stones can be pushed up into the lumen of the gallbladder, and no apparent stone debris attached to the mucosa of the ampulla, cholecystolithotomy can still be performed. However, if stone is incarcerated in the cystic duct, LC was performed due the difficulty in extracting the stone out. Therefore, although cholecystolithotomy is beneficial to the patients, for some cases, cholecystectomy is the better choice.

In conclusion, gallbladder preserving cholecystolithotomy is a safe procedure without major complications, while cholecystectomy complicates with diarrhea in high percentage. LCCC group takes more time than LC group without differences on postoperative hospital stay and other clinical data. LCCC has a low recurrence rate in five years and deserve further study.

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