FACULTAD DE MEDICINA
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TRABAJO FIN DE GRADO

Comparación de resultados del tratamiento de la coledocolitiasis vía laparoscópica o endoscópica

Laparoscopic versus endoscopic approach in the management of choledocholithiasis

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1.RESUMEN

INTRODUCCIÓN: El tratamiento de la coledocolitiasis ha sido objeto de estudio en los últimos años debido al avance de las distintas opciones terapéuticas, que incluyen tratamiento médico, endoscópico y quirúrgico. Las guías internacionales no han reflejado hasta el momento la superioridad de una técnica frente a las demás, por lo que no existe un consenso de actuación ante esta patología. Actualmente, la exploración de la vía biliar y la colecistectomía laparoscópicas frente a la combinación de CPRE con colecistectomía laparoscópicason las vías más desarrolladas, por lo que con este estudio, se pretende comparar estos dos abordajes y analizar sus resultados en términos de resolución de la coledocolitiasis y complicaciones asociadas.

OBJETIVO: Comparación del manejo laparoscópico y el abordaje endoscópico en términos de resolución de la coledocolitiasis y morbilidad asociada

MÉTODOS: Estudio restrospectivoobservacional en el que se comparan los resultados de la realización de exploración de la vía biliar y colecistectomía laparoscópica versus CPRE y posterior colecistectomía laparoscópica en una cohorte de 119 pacientes diagnosticados de coledocolitiasis, durante los años 2008 a 2016, en el Hospital Universitario Marqués de Valdecilla de Santander.

RESULTADOS: Tras revisar 119 pacientes, de los que 82 fueron intervenidos por la vía laparoscópica y 37 por vía endoscópica, no se observan diferencias significativas entre ambas modalidades en términos de resolución de la coledocolitiasis y complicaciones asociadas.

CONCLUSIONES: Estos resultados coinciden con los reportados en la literatura, por lo que no existen recomendaciones que apoyen la realización de una técnica frente otra, sino que la elección del abordaje terapéutico se determina por la experiencia y los recursos locales.

ABSTRACT

BACKGROUND: Choledocholithiasis therapeutical approach has been studied by literature in recent years, due to the development of the available techniques, which include medical, endoscopic and surgical treatment. International guidelines have not proved the superiority of one technique compared to the other. Therefore, there is no consensus in the management of this pathology. Nowadays, laparoscopic common bile duct exploration with following laparoscopic cholecystectomy and ERCP and posterior laparoscopic cholecystectomy are the more extended approaches. This study compares these two procedures and analyzes their results in terms of choledocholithiasis resolution and related complications.

OBJECTIVE: To compare the laparoscopic approach and the endoscopic management in terms of choledocholithiasis resolution and rate of associated complications.

METHODS**:** Our study is a retrospective analysis of a 119 patient cohort with confirmed choledocholithiasis that underwent ERCP/ES + LC or LC+LCBDE at Hospital UniversitarioMarqués de Valdecilla(Santander) during a 8 year period, from 2008 to 2016.

RESULTS: We reviewed 119 patients: 82 of them weremanaged with laparoscopy and 37 with endoscopy. No significant differences were found in terms of choledocholithiasis resolution and associated complications.

CONCLUSION: We observed similar outcomes to the literature. Therefore, therapeutical management choice depends on local expertise and resources.

2. INTRODUCTION

2.1 BILIARY SYSTEM ANATOMY

The gallbladder is a pear-shaped organ that extends from the right extremity of the right hepatic lobe to the inferior border of the liver. It is 7 to 10 cm long and 3 to 4 cm broad, and can hold 30 to 50 ml of bile. It is divided into a fundus, body, infundibulum and neck. The neck is the tapered segment of the infundibulum that is narrow and joins the cystic duct.Its blood supply depends on the cystic artery, which can be originated from the right hepatic (most commonly), left hepatic or the common hepatic artery. The venous drainage is through the cystic vein, which drains into the portal vein.

The union of the right and left hepatic ducts forms the common hepatic duct. The cystic duct joins the common hepatic duct to form the common bile duct that drains bile into duodenum. This comprises the extrahepatic biliary system. This confluence takes place at the right of the hilum of the liver, anterior to the portal venous bifurcation and overlying the origin of the right branch of the portal vein. There are some variations in the drainage of the intrahepatic ducts into the cystic duct that are important to note during cholecystectomy.

The common bile duct, also named ductus choledochus, is divided into supraduodenal, retroduodenal, pancreatic and intraduodenal segments. The supraduodenal part lies in the free border of the hepatoduodenal ligament. The pancreatic segment is related to the head of the pancreas, although it can run entirely retropancreatic or travel through its parenchyma.

The diameter of the common bile duct is often an indicator of biliary pathology. Its normal range goes from 4 to 13 mm. Although it depends on the technique used to examine it, a diameter up to 6 mm is considered normal.

The entrance of the common bile duct in to the duodenum is placed approximately 8 cm from the pylorus in the second part of the duodenum. The site entry is marked by a papilla (Papilla of Water). The main pancreatic duct of Wirsung joins the common bile duct and forms a common channel in 85% of individuals. This channel is covered by sphincter of Oddi, which is generally a continuous smooth muscle structure that is subdivided in several parts.

The blood supply to the common bile duct originates from the retroduodenal artery, right hepatic artery, cystic artery, gastroduodenal artery and the retroportal artery. The venous drainage corresponds to the respective veins of the arteries mentioned above.[1]

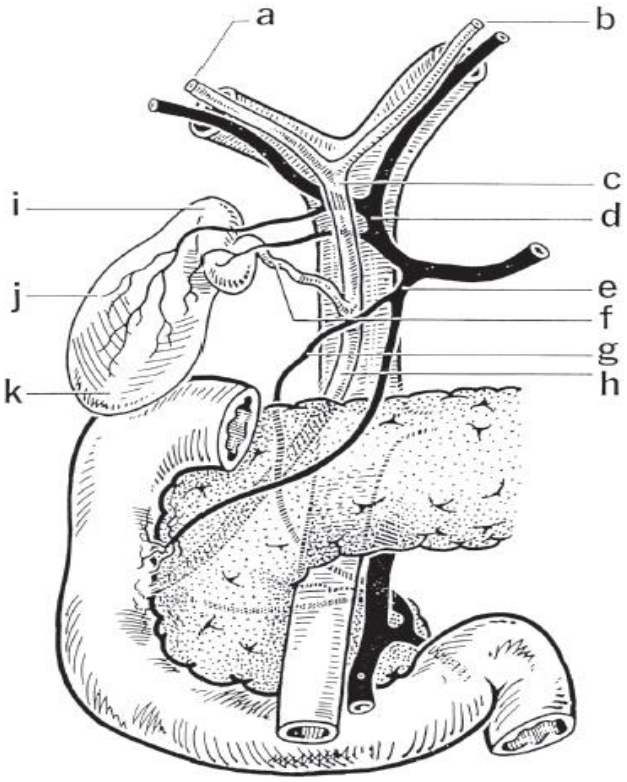

Image 1: Extrahepaticbiliar system anatomy: (a) right hepatic duct, (b) left hepatic duct, (c) common hepatic duct, (d) hepatic artery, (e) gastroduodenal artery, (f)cystic duct, (g)retroduodenal artery, (h) common bile duct, (i) neck of the gallbladder, (j) body of the gallbladder, (k)fundus of the gallbladder.[1]

2.2 EPIDEMIOLOGY

The prevalence of gallbladder lithiasis isapproximately21.9 million worldwide, being 14.2 of them women. In Europe it is reported to vary between 5.9% and 21.9% of the general population [2].

About 10%to 33% of patients with symptomatic cholelithiasis present common bile duct (CBD) stones[3,4] and, at the time of surgery, 11% to 21% of patients with cholelithiasis also have CBD stones. After cholecystectomy, it is reported that, in 1% to 5% of the patients, undetected lithiasis remain in the biliary tract.

Epidemiologic data have been studied in European and American population and they revealed a notorious variation in gallstone prevalence between different ethnic populations, being Western Caucasian, Hispanic and Native American populations the countries with higher rates of cholelithiasis. On the other hand, African Americans seem to have the lowest prevalence of gallbladder stones.

Apart from the ethnic variations, multiple risk factors have been studied. Most CBD stones are originated in the gallbladder and, therefore, the main risk factors of choledocholithiasis are the same as those of cholelithiasis, which are summed up in Table 1.

AGE

FEMALE SEX

GENETIC

- Pima Indians and Native Americans
- Chileans

PREGNANCY

OBESITY

RAPID WEIGHT LOSS

- Very lowcalorie diet
- Surgery therapy of morbid obesity

CIRRHOSIS

HEMOLYTIC ANEMIAS

HYPERTRIGLYCERIDEMIA

MEDICATIONS

- Estrogen and oral contraceptives
- Clofibrate
- Ceftriaxone
- Octreotide

TERMINAL ILEAL RESECTION

GALLBLADDER STASIS

- Diabetes mellitus
- Total parenteral nutrition
- Postvagotomy
- Octreotide or somatostatinoma
- Spinal cord injury

REDUCED PHYSICAL ACTIVITY

Table 1: Risk factors of choledocholithiasis[8]

As it is described in TABLE 1 gallstone disease is a multifactorial process, but current guidelines highlight itsundoubtedly association with ageing. What is more, up to one third of the population over 70 years of age will have gallstones [5].

The greatest prevalence of choledocholithiasis in female might be explained by the increased biliar saturation due to estrogenic action on the cholesterol hepatic metabolism. Estrogenic activity would be responsible as well of the higher risk of CBD stones during pregnancy.

In contrast, there are some protective factors that have been reported, such as statins, ascorbic acid, coffee, vegetable protein and nuts and poly- and monounsaturated fats.

2.3 ETIOPATHOGENESIS

The gallbladder stores hepatic bile and then releases it into the duodenum to contribute to fat absorption. This secreted bile is 10 times more concentrated than when first excreted by the liver, caused by active sodium transport by the gallbladder epithelium. Bile stasis due to decreased gallbladder motility produces stone formation, and the migration of these calculi can lead to CBD obstruction, causing choledocholithiasis, which can be silent or symptomatic.

According to the origin of the stone, we can classify CBD stones in primary (Table 2) or secondary. Over 90% of stones within the bile ducts are secondary in nature.Primary CBD stones are “in situ” produced stones and they are browned pigment colored, mostly formed of bilirrubin.They are usually classified according to their location as

intrahepatic, extrahepatic or ampullary.These“de novo” lithiasis (pigment stones) are the result of an impediment to the flow of bile within the biliary tree, and appear mostly in the following situations: hepatobiliar parasitism and recurrent chronic cholangitis, genetic abnormalities such as Caroli disease, duct dilatation, stenosis or sclerosis and MDR3(ABCB4) gene defect that may diminish biliary phospholipidic secretion [6,7].

- Prior biliary surgery
- Parasitic infection
- Iatrogenic stricture
- Biliary-enteric anastomosis
- Caroli’s disease
- Sclerosis cholangitis
- Stenosingpapillitis
- Periampullary duodenal diverticulum

Table 2: Risk factors for primary CBD stones

Secondary stones are those that migrate from the gallbladder and are mostly constituted by cholesterol. Cholesterol gallstones represent approximately 70% of gallstones found in patients in the Western world (Table 3). Several risk factors have been reported to be responsible of this migration: long time cholelithiasis, small diameter calculi, a wide cystic duct with incompetent valves or ageing are the most remarkable [8].

TYPE	**ASSOCIATED CHARACTERISTICS**
Cholesterol	Obesity, parity, age, hyperlipidemia
Pigment	Hemolysis, cirrhosis, total arenteral nutrition
Mixed	Combination of above, ileal resection
Calcium carbonate	Opaque, infection, least common

Table 3: Types of secondary choledocholithiasis

Once in the CBD, stones may migrate to the duodenum or remain in the choledochus depending on the diameter of the distal CBD at the Vater papilla. Bilostasis may lead to bile infection and ascending cholangitis, whereas bile or pancreatic juice flow problems at the merging of the CBD and the Wirsung duct are responsible to trigger acute biliary pancreatitis.

2.4 CLINICAL PRESENTATION

The clinical presentation of choledocholithiasis may vary widely, as CBD stones may be asymptomatic (approximately half of the cases) or clinically e)xpressed with various symptoms, ranging from colicky pain to potentially life-threatening complications such as cholangitis and pancreatitis [2].

As previously stated, in 10% cases of intraoperative cholangiography during cholecystectomy, CBD stones are found, and in most cases, they remain silent. Nevertheless, patients with diagnosed choledocholithisis frequently have a medical history of biliary colic episodes.

When not clinically silent, choledocholithiasis can be manifested as biliary colic, with similar characteristics as the pain produced by gallbladder stones: right upper quadrant or epigastric constant pain that may be associated with heavy meals, that frequently lasts more than 30 minutes and up to several hours, and does not depend on the body position. Hyperbilirrubinemia caused by biliary obstruction justifies the jaundice, called obstructive jaundice, which leads to dark urine (choluria) and lightening of the stools. This occurs because of the accumulation of direct bilirrubin.

- Abominal pain
- Jaundice
- Choluria
- Lithtening of the stools
- Cholangitis (Charcots triad)
- Itching skin
- Nausea and vomiting

Table 4: Choledocholithiasis. Main clinical features.

When there are associated complications, such as cholangitis, fever is another common symptom that is part of Charcot's triad, constituted by jaundice, right upper quadrant pain and fever (table 4). If hypotension and mental status alterations are associated, a biliary source shock should be suspected, and Charcot triad is known as Reynolds pentad [9].

In a prospective study carried out by Manimaran et Al. in a 115 patient cohort [10], abdominal pain was the main symptom in 60, 86%, jaundice in 38,26%, fever in 36,52%, Charcot triad in 33,04%, biliary pancreatitis in 5,21% and 3,47% were asymptomatic.

2.5 DIAGNOSIS

2.5.1. *Preoperative evaluation*

CBD stones are diagnosed with a combination of laboratory tests and imaging studies.Several studies concluded that the initial assessment of patients with suspected CBD stones should be based on clinical features, liver function tests and abdominal ultrasound (US) findings [8,11].

- Patient history and physical examination

Asking the patient about symptoms of CBD stones (colicky pain, jaundice, cholangitis, pancreatitis…) or biliary colic in the past is the first line diagnostic approach. It is also important to look for risks factors of presenting choledocholithiasisor its complications.

Physical examination may not be very revealing, showing scratching signs in some cases, due to the itching skin produced by the hyperbilirrubinemia.

-Laboratory tests

Laboratory data may be normal in as many as a third of patients with choledocholithiasis [8]. However, in liver biochemical tests, abnormal cholestasis indexes, including gamma-glutamil-transpherase (GGT), direct bilirubin and alkaline phosphatase (AP) suggests CBD stones. In long-time cholestasis, AST and ALT may be also altered.

However, Costi et al (2016) study states that the positive predictive values for abnormal bilirubin, AP or GGT range from 25-50% only.

Haemogram does not provide any particular result, apart from leukocytosis in cases of acute inflammation processes, such as associated cholecystitis, cholangitis or pancreatitis due to biliary obstruction.

Lastly, a CA 19.9 increase has been observed in some cases of cholangitis.

-Transabdominal US [5,12]

US examination is the first line imaging study, as it is a non invasive, widely available, portable and non-expensive screening test. However, it is highly operator dependent.

In contrast to gallbladder stones, which are frequently directly detected by US, CBD ultrasonographic examination is based on indirect signs suggesting the presence of stones, since there is often overlying bowel gas. As a result, US can detect a dilated extrahepatic bile duct, typically a CBD>6 mm, which is an indirect sign of choledocholithiasis.

The sensitivity of US for detecting CBD stones, according to various studies, varies from 55 to 91%. Such wide range proves that a negative US does not rule out choledocholithiasis.

Once the initial workup has been done, “second line” examinations should be used. These tests can be endoscopic or non-endoscopic methods.

-Computed tomography (CT)

It is considered more accurate than US in identifying CBD stones, although it is not as accurate as Magnetic Resonance Cholangiopancreatography (MRCP). The literature regarding CT for diagnosis of CBD stones is heterogeneous ant it is usually not considered a definitive test [12].

Its sensitivity can be as high as 95,5%, but many gallstones have similar density to surrounding bile and lack calcium, which limits its effectiveness.

CT scan often offers the possibility of measuring the CBD diameter and, with intravenously administered contrast agents and high resolution helical scans and three dimensional reconstructions, which are evolving nowadays, its efficacy may improve.

-Magnetic Resonance Cholangiopancreatography (MRCP)

MRCP is considered nowadays the most accurate non invasive (non-endoscopic) procedure for the detection of CBDS, with 85%.92% sensitivity and 93%-97% specificity [2]. This technique uses T2 images to visualize the filling effects or stenosis in the biliary tree.

Using a contrast agent on T1 weighted images may give additional information about the degree of obstruction, and allows a better CBD visualization in patients with ascites.

Its sensitivity is often compared with EUS (Endoscopic Ultrasound) sensitivity in several meta-analysis, showing no significant differences. However, it is important to point that MRCP is a non-invasive technique and it has prove to be less sensitive than EUS for detecting CBD stones smaller than 6 mm. Another specific issue of this technique is its limitations in morbid obesity or claustrophobic patients and its suboptimal availability in non-tertiary care centers.

-Endoscopic Ultrasound (EUS)

EUS has proved to be an excellent option with sensitivity of 95% and specificity of 97% in detecting CBD stones. It uses an USE probe mounted on the tip of an endoscope. Therefore, it is not appropriate in patients with postsurgical anatomy, since it requires approximation of the US probe to the CBD.

EUS main advantages are its sensitivity for stones smaller than 5 mm and the fact that it does not require ionizing radiation [12]. The choice between EUS and MRCP is based on the resource availability and local experience.

-Endoscopic Retrograde Cholangiopancreatography (ERCP)

ERCP has a diagnostic and therapeutic role in CBD stones, and has been the gold standard for their preoperative diagnosis, [2,5] with a 75%-93% sensitivity and 100% specificity.

The procedure consists on cannulating the ampulla of Vater with injection of contrast under fluoroscopy, and detecting filling defects. It has complication rates of 8 to 12% which makes this technique only appropriate for patients with high probability of choledocholithiasis, due to both invasiveness and the ability to treat if CBD stones are found.

However, ERCP is being abandoned as a diagnostic tool since is not cost-effective for intermediate risk cases. Compared to EUS and MRC, ERC accuracy is suboptimal and apart for involving X-ray exposure and the invasiveness of endoscopic procedures, it has important technique-related mortality/morbidityconsisting on pancreatitis, cholangitis, perforation and bleeding. What is more, Karaliotas et al. observed that the following circumstances may lead to ERCP failure: stone impaction, gastrectomy or Roux-en-Y anatomy, recurrent bile duct stones after prior open exploration of the CBD and biliodigestive anastomosis, periampullary diverticula and Mirizzi syndrome [13].

Therefore, ERCP is progressively adopting a therapeutical function in CBD stones, while its diagnostic role is being substituted by MRC or EUS[5].

2.5.2.*Intraoperative evaluation*

-Intraoperative colangiography (IOC)

Since laparoscopic cholecystectomy is nowadays a routine procedure, intraoperative bile duct assessment with IOC is a useful tool, although it is under debate its cost-effectiveness when performed systematically or in selected population [2].

IOC enables the identification of CBD stones with dynamic fluoroscopic imaging. This technique should show the cannulation of the cystic duct, filling of the left and right hepatic ducts, CBD and common hepatic duct diameter, the presence or not of filling defects and free flow of contrast into the duodenum. If these findings are not observed, a biliar obstruction or abnormality should be suspected.

Its sensitivity and specificity are 98% and 94% respectively in experience hands, and it is considered a safe technique, but it does prolong operative time and literature has

not shown significant differences in the rates of ductal injury between routine and selective IOC, but is has clearly less rates of pancreatitis in contrast to ERCP.

In conclusion, in cases where choledocholithiasis is not proven, IOC during laparoscopic cholecystectomy is a better choice than precholecystectomy ERCP assessment of the bile ducts.

- Laparoscopic US

Laparoscopic ultrasound has not yet become popular worldwide, but it is based on the fact that US is more effective when the probe is placed nearer to the CBD. It is reported to have a sensitivity of 92%-95% and a specificity of 99%-100%.

It is less invasive than IOC and the operative times are shorter than IOC, although it needs expertise and specific instrumentation, and, sometimes, it is difficult to identify bile duct anatomy.

2.5.3.*Diagnosis approach*

Literature has not shown any consensus about the CBDS diagnosis algorithm, mainly due to the constant arising of techniques and the singular behaviour of this pathology. In up to 20% of the cases of biliary lithiasis gallbladder stones are associated with CBDS, which are asymptomatic in up to one half of cases. About 10%to 33% of patients with symptomatic cholelithiasis present common bile duct (CBD) stones [2,3] and, at the time of surgery, 11% to 21% of patients with cholelithiasis also have CBD stones not previously detected. Since CBDS can lead to serious complications, they must be diagnosed and treated.

Despite the wide variety of examinations and techniques available nowadays, two main open issues remain without a clear answer:how to cost effectively diagnose CBDS and, when they are finally found,how to manage them. Nevertheless, the most common imaging techniques used to identify CBDS are, although accurate, expensive and invasive. These reasons contraindicate their systematic, pre-cholecystectomy use, unless there is a clear indication. In order to select the most appropriate management, patients may be classified preoperatively into high, moderate or low risk groups. This evaluation is made with non-invasive techniques such as clinical features, biochemical tests and abdominal ultrasound (US).The American Society for Gastrointestinal Endoscopy (ASGE) guidelines [14]proposes this stratification:

Predictors of choledocholithiasis	
Very strong	
CBD stone on transabdominal US	
Clinical ascending cholangitis	
Bilirubin>4 mg/dL	
Strong	
Dilated CBD on US (>6 mm with gallbladder in situ)	
Bilirubin level 1.8-4 mg/dL	
Moderate	
Abnormal liver biochemical test other than bilirubin	
Age older than 55 years	
Clinical gallstone pancreatitis	
Asigning a likelihood of choledocholithiasis based on clinical predictors	
Presence of any very strong predictor	High
Presence of both strong predictors	High
No predictors present	Low
All other patients	Intermediate

Table 5: ASGE estimation of risk of carrying CBD stones [14]

2.6 TREATMENT

The development of new techniques such laparoscopy and endoscopy in the field of biliary tract and the variations due to local expertise and time of CBD stones diagnosis (preoperative, intraoperative, postoperative) makes the treatment choice a complex and controversial issue. The concomitant presence of cholelithiasis in CBD explains that there is always a formal indication for cholecystectomy, preferably laparoscopic cholecystectomy (LC).

The CBD assessment consists on stone clearance that can be performed with surgery (laparotomy or laparoscopy), endoscopy or lithotripsy.

Nowadays, the current management of CBDS consists on endoscopic sphincterotomy (EST) followed by laparoscopic cholecystectomy (LC), although laparoscopic exploration of the CBD is becoming more popular.

We can classify the different options on endoscopic procedures, surgical procedures and lithotripsy.

Endoscopic procedures
- ERCP+ES
- Endoscopic papillary balloon dilatation (EPBD)
Surgical procedures
- Open surgery
- Laparoscopy
- Emerging mini-invasive surgical techniques
Lythotripsy

Table 6: Management options for CBDS

2.6.1.*Endoscopic procedures*:

Endoscopy is able of treating 90% of choledocholithiasis [12].Endoscopic sphincterotomy (ES) and endoscopic papillary balloon dilation (EPBD, associated with stone extraction, are the primary treatment of CBD stones.

- ERCP+ES [14]

There is a debate about the time of this procedure, since ERCP can be performed before, during or after cholecystectomy. Costi et al. [2] stated that "…*performing ERCP before surgery raises questions regarding patient selection because systematic preoperative ERCP before LC means an intolerably great number of unnecessary and potentially harmful procedures…".* However, preoperative ERCP and LC is the preferred option in the management of CBDS.

ES uses electrocautery to cut the muscles of the Oddi sphincter. Papillotomy is often used to refer to the same process, although it refers to severing the superficial sphincter of the duodenal papilla. Deep cannulation of the CBD under visual and fluoroscopic guidance is the first step before ES is performed.

Sphincterotomy is usually performed after deep cannulation of the CBD has been accomplished. This is possible under visual and fluoroscopic guidance.

ERCP begins with the insertion of the duodenoscope into the second part of the duodenum and the identification of the major papilla. The cannulation of the major papilla is followed by the placement of the sphincterotome, tailoring it to the incision length. Finally, the application of an electrical current to the sphincterotome wire cuts the papilla and CBDS extraction is performed by Dormia Basket or balloon.

Endoscopic sphincterotomy success rate is reported to exceed 90%, although large series have recently shown 5%-9,8% morbidity and 0,3%-2,3% mortality, mostly due to acute pancreatitis, bleeding and perforation. Long term complications include papillary stenosis, cholangitis, and recurrent choledocholithiasis.

This technique means a "two step management" of choledocholithiasis, needing a second surgical procedure to treat gallstones (LC). However, the great advantage is that if it is succesfull, LC may complete a mini-invasive management of CBD stones. If it is not, usually a second ERCP is needed or LCBDE is needed, meaning another invasive apprach.

- ENDOSCOPIC PAPILLARY BALLOON DILATION (EPBD)

Endoscopic papillary balloon dilation can be an option for the management of difficult biliary stones [2,9]It minimizes the risk of bleeding during the sphincterotomy, so it is a

very attractive option for patients with high risk of bleeding or in those with altered anatomy in which a full sphincterotomy cannot be achieved.

EPBD is performed with a guidewire into the CBD and a balloon catheter guided into the wire. Then, the balloon is inflated until it reaches a diameter of approximately 20 mm.

Although it has shown to have a minimal risk of bleeding, rates of stone removal seem to be lower with this technique in comparison with full sphincterotomy. However, it is usually performed in older patients or in those who are at risk of infection or affected by coagulopathy.

2.6.2. *Surgical procedures*

Since the early eighties, the arising of endoscopic techniques has radically changed the surgical management of choledocholithiasis. Until then, open cholecystectomy and open exploration of common bile duct was the main procedure, and included duodenotomy and sphincterotomy or bilio-enteric anastomosis.

Recent advances in the surgical field have introduced mini-invasive techniques, such as single incision laparoscopy or natural orifice translumental endoscopical surgery or robotic surgery. These techniques, that are nowadays infrequent, illustrate the possible future management of this pathology.

- OPEN SURGERY [10]

As already said, open surgery via laparotomy was the main option until 30 years ago. This technique, although it is considered the last resource in CBDS management, has prove to have higher rates of stone removal than ERCP [2]with no increase if morbidity/mortality.

A recent study carried out by Halawani et al[15]compared laparoscopic versus laparotomy approach and showed statiscally significantly higher rate of mortality and overall complications in those patients that underwent open CBD exploration. However, retained CBD stones and their complications were 2.8 times more likely to occur in the laparoscopic group than in the open group.

Open CBD exploration is an invasive technique, so it would be logical to expect more morbidity, mortality, return to operating room or even surgery-related death. However, the lack of laparoscopic expertise and the necessary equipment explains why many surgeons keep performing open CBD exploration.

The abdomen is most commonly opened through a incision in the right upper quadrant. Stones may be extracted using manual manipulation of the CBD or with balloon extraction with biliary Fogarty catheters, clearing the proximal duct before the

distal duct. Choledochoscopy can be used if the balloon technique fails. The procedure ends with the placement of a T-tube into the duct and its extraction out of the abdomen through a separate stab incision.

Complications, apart from the above mentioned morbidity, include bile duct leak (2%-6%), subhepatic abscess (0,7%) and retained stones (3%-6%).

Nowadays, indications for performing open CBDE are:

- Patients with CBD stones who are undergoing open cholecystectomy
- Patients who have failed or suffered complications from laparoscopic CBD exploration
- Patients with severe inflammation in the triangle of Calot
- Settings where laparoscopic equipment, experience, and/or resources are limited

- LAPAROSCOPY

Since 1991, CBD exploration may be performed laparoscopically. In expert hands, it is reported to be as effective as ERCP in stones clearance, although the technical difficulty and the need of very experienced surgeons and long operating time (an average of 5 hours), make this technique the preferred one only in very specialized environments.

LCBDE may be performed via choledochotomy or via transcystic exploration, and literature describes that the most extended is the transcystic approach:

- **Transcystic common bile duct exploration (TCBDE)**
  It is the preferred technique for most patients with stones smaller than 10 mm and a small bile duct. It has proven to be fast and safe, and it is indicated in the following situations:
    - CBD diameter <6 mm
    - Stone location distal to the cystic duct/CBD junction
    - Cystic duct diameter >4 mm
    - Fewer than 6 to 8 stones within the CBD
    - Stones smaller than 10 mm

  The procedure begins with the flushing of the CBD that can be facilitated by dilatation of the cystic duct with a balloon. If the duct cannot be cleared with flushing and balloon catheters, either transcystic choledochoscopy or fluoroscopically-guided wire basket retrieval may be employed.
  Transcystic stone clearance may be altered by abnormal anatomy, proximal stones (in the hepatic duct), strictures and large or numerous stones.

- **Choledochotomy**

  It requires more technical skills than the transcystic option and it may be performed when this latter has failed. The open bile duct can be managed with closure over a T-tube, exteriorized transcystic drainage or without endoluminal drainage. Several studies have compared primary closure versus T-tube and they have shown similar rates of complications, with shorter operating times with primary closure.

  This technique is recommended in:

    - Failed laparoscopic transcystic exploration or preoperative endoscopic stone extraction
    - Narrow cystic duct
    - Dilated CBD
    - Large stones
    - Multiple stones
    - Stone location proximal to the cystic duct or CBD junction

- EMERGING MINI-INVASIVE SURGICAL TECHNIQUES

They include single incision laparoscopy (SIL), natural orifice translumenal endoscopy surgery (NOTES) and robotics. There have not been very analyzed by literature and therefore, very little information is known about them. However, a recently study about robotic hepatobiliary surgery in the CBD exploration has revealed that robotic laparoscopic exploration of the CBD means longer operating time and a shorter median hospital stay compared to open surgery [16].

2.6.3.Lythotripsy

It was introduced in 1982 and it is often used when the standard methods of managing CBDS fail. It cannot be considered a radical treatment for CBDS, since it does not eliminate the main origin of choledocholithiasis, which is the gallbladder. Therefore, it does not allow for avoiding cholecystectomy.

There are several ways of performing this technique (endoscopical mechanical lithotripsy, endoscopic electrohydraulic lithotripsy, endoscopic laser lithotripsy, extracorporeal shock-wave) and none of them is considered as being the first line treatment for CBDS.

2.7 COMPLICATIONS

The two main complications associated with CBDS are acute cholangitis and acute pancreatitis.

Acute pancreatitis [2,9]

The incidence of acute pancreatitis caused by gallstones seems to be increasing. In the US a study showed that one-third of cases of acute pancreatitis among adults are caused by gallstones [17]. Furthermore, in 4-8% of patients with cholelithiasis, stones migrate into the CBD causing acute pancreatitis as they pass into the duodenum or impact in the sphincter of Oddi.

Gallstone migration, even of small lithiasis, is frequently preceded by a period of biliary obstruction. Diagnosis is based on biochemical tests (hyperlipasemia or hyperamilasemia, elevated aminotransferase levels, cholestasic parameters) and imaging tests, such us US, ERCP or ERCP. EUS is superior to all other tests at detecting CBD stones in cases of acute biliary pancreatitis (sensitivity 97%, specificity 95%), because it can detect stones smaller than 5 mm, which are those that often cause acute pancreatitis.

Treatment of acute biliary pancreatitis is controversial, since the timing of cholecystectomy and the choice of procedures for clearing associated CBD stones remains unclear. In cases of severe pancreatitis with multisystem organ failure, inmediate ERCP to clear biliar obstruction is indicated, as well as supportive care. However, when CBD stones associated pancreatitis is mild and self-limited, the recommendations state that cholecystectomy should be performed after symptoms have subsided and laboratory tests normalized, using during the same hospital admission. CBD clearance can be perfomed intraoperative laparoscopically or preoperative, with ERCP.

Acute cholangitis:

Cholangitis is a serious complication of gallstones, with high rates of mortality and morbidity. After broad spectrum antibiotics have been applied, biliary descompression is the standard treatment. Due to the heterogeneous clinical presentation of cholangitis, in mild to moderate disease, billiarydescompression may be planned by endoscopy or laparoscopy, whereas in severe cholangitis or sepsis, urgent endoscopic sphincterotomy should be performed even if CBD stones are not found during ERCP. Definite stone removal can then be performed after the acute episode has subsided.

3. OBJECTIVES AND HYPOTHESES

Our main hypothesis isthat laparoscopic management of choledocholithiasis is superior to endoscopic approach in terms of stone removal and associated complications.

The main objective of this study is to compare the most extended two therapeutical strategies for CBDS: the “endoscopic procedure”, which includes Endoscopic Retrograde Cholangiopancreatography with Endoscopical Sphincterotomy and posterior Laparoscopic Cholecystectomy (ERCP/ES +LC) and the “laparoscopic management”, which consists on Laparoscopic Common Bile Duct Exploration and Laparoscopic Cholecystectomy (LCBDE+LC). The strategies will be compared in terms of morbidity and retained stones rates.

4. METHODS

This was an observational retrospective single center study, covering an 8 year period, from February 2008 to April 2016, with a patient follow-up of an average of 4 months.All patients were diagnosed of choledocholithiasis and had a formal indication of stone removal, which was performed with LC+LCBDE (**GROUP I**) or preoperative ERCP+ES followed by LC (**GROUP II**).

4.1 PATIENT CHARACTERISTICS:

We studied 119 patients with diagnosed CBD stones who were candidates for stone extraction at Hospital UniversitarioMarqués de Valdecilla.A 37-patient cohort was treated with ERCP/ES+LC (GROUP I) and a 82-patient cohort was managed with LC+LCBDE (GROUP II).

Diagnosis was performed with clinical, laboratory or radiographic and US findings suggestive of CBD stones. In most of them, a MRCP was performed to confirm diagnosis and observe the CBD dilatation.

All patients were submitted to each technique on a schedule basis, thus none of the patients was operated with emergency surgery or endoscopy.

Patients with malignant obstruction of CBD or with hepatic transplantation were excluded from the study, as well as those in which LC was not performed because of high surgical risk.

IOC was performed in all patients from GROUP I.

4.2 DATA

The recorded data of all the studied population included the following issues:

- **GENDER**
- **AGE**
- **BMI**
- **CLINICAL FEATURES**
  - Abdominal Pain
  - Jaundice
  - Choluria
  - Fever
  - Pancreatitis
- **TB (mg/dL)**
- **ABDOMINAL US FINDINGS**
  - Cholelithiasis
  - Cholecystitis
  - CBD Dilation
  - Choledocholithiasis
- **MRCP FINDINGS**
  - Cholelithiasis
  - Cholecystitis
  - CBD Dilation
  - Choledocholithiasis
- **CBD DIAMETER (mm)**
- **ASA**
- **DIAGNOSIS TO TREATMENT TIME (days)**
- **LC**
  - Date
  - Reconversion
  - Complications
- **RESIDUAL CHOLEDOCHOLITHIASIS**
- **MANAGEMENT OF RESIDUAL CHOLEDOCHOLITHIASIS**
- **FOLLOW-UP PERIOD (months)**
- **DAYS OF HOSPITALIZATION**
- **COMPLICATIONS**
  - Bleeding
  - Infection
  - Fistula/Perforation
  - Acute Pancreatitis

Table 8: Recorded data of the total sample

Apart from these data, specific features were recorded from each group:

GROUP I

- **LCBDE+LC DATE**
- **CBD APPROACH**
- **CHOLEDOCHOSCOPE**
- **CHOLANGIOGRAPHY**
- **KEHR DRAINAGE**
- **COMPLICATIONS**
- **TRANS-KEHR CHOLANGIOGRAPHY**

GROUP II

- **ERCP**
  - Date
  - Procedure
  - Biliary Stent Prosthesis
  - Resolution
  - Complications
- **ERCP-LC PERIOD**

Table 9: Additional recorded data from GROUP I and GROUP II

4.3OUTCOMES AND DEFINITION OF SUCCESS

Primary outcome was based on CBD clearance rate, complications and normality of the follow-up tests.

Definition of success varies depending on the studied group. In ERCP/ES+LC group success was defined by the absence of LC reconversion to laparotomy, absence of residual choledocholithiasis and the resolution of the ERCP. The need of a second ERCP is considered as a treatment failure.

By contrast, in LCBDE+LC group, success is defined by the absence of LC reconversion to laparotomy, the absence of residual choledocholithiasis, the normality of post-LCBDE trans-Kehr cholangiography (with no filling defects) and the normality of consecutive follow-up MRCP in those patients that did not have Kehr drain.

ERCP resolution was defined by the absence of repletion defects in final cholangiography and the absence of a second ERCP. In some ERCPS, a prosthesis was implanted.

4.4FOLLOW-UP EVALUATION

Follow-up of the 119 patients was performed with clinical tests and imaging studies, such as US or MRCP. All patients were reviewed one month after the intervention. Biliary-related symptoms, complications or deaths during hospitalization are recorded.

4.5 STATISTICAL ANALYSIS

A descriptive analysis of each group and the total sample was performed. Quantitive values following a normal distribution were described by mean and standard deviation. For qualitive variables, absolute frequencies and corresponding percentages were calculated. Differences between groups were performed using the Chi-square, ANOVA and T test. For all these tests, a P value <0, 05 was considered statistically significant.

5.RESULTS

5.1: Descriptive analysis:

Demographic and clinical characteristics are presented in Table 10:

	GROUP I (ERCP/ES+LC) (n=37)	GROUP II (LC+LCBDE) (n=82)	*p* value
AGE	69,62	65,01	NS (0,19)
SEX			S (0,012)
- M	23	31	
- F	14	51	
BMI	28,24	28,65	
ASA			
- I	10	21	
- II	18	52	
-III	8	8	
- IV	1		

Table 10: Demographic patient characteristics. BMI, body mass index; ASA, American Society of Anesthesiologist physical classification system.

As described in Table 10, there were significant differences between both groups regarding sex: 62,18% of GROUP II was constituted by women.By contrast, age characteristics were comparable.

- CLINICAL PRESENTATION

Symptoms:

	GROUP I (N=82)	GROUP II (N=37)	TOTAL (n=119)
Abdominal pain	64 (78,8%)	34 (91,9%)	98 (82,35%)
Fever	12 (14,6%)	8 (21,6%)	20 (16,80%)
Jaundice	35 (42,7%)	9 (24,3%)	44 (36,97%)
Choluria	16 (19,5%)	11 (29,7%)	27 (22,68%)
Pancreatitis	4 (2,5%)	0	4 (3,36%)

Table 11:Clinical features of each group

As shown in Table 11, the most common symptom in both groups was abdominal pain, followed by jaundice and choluria. Several studies have studied the clinical presentation of CBD stones: Hu et al. analyzed 443 patients with pancreatobiliary diseases and found that the most frequent clinical presentation of all groups was biliary colic [18].

- LABORATORY TESTS

Total billirrubin values were analyzed at the time of hospital entrance and the following results were observed:

	Total population (n=119)
Total billirubin (n=119)	3,87 mg/dL±3,29

Table 12: Total bilirrubinvalues

- CBD DIAMETER

The definition of CBD dilatation is a matter of discussion, since suggested "normal limits" vary widely, ranging from 5 to 11 mm. For example, Mohamed et al. prospective analysis considered a dilated CBDwhen CBD was observed to be more than 8 mm. [19]. We have defined CBD dilatation >6 mm.

	Total population (n=119)
CBD diameter	12 mm ±3,45

Table 13: CBD diameter

- US FINDINGS

	GROUP I(N=82)	**GROUP II (N=37)**	**TOTAL (n=119)**
CHOLELITHIASIS	70 (87,5%)	33 (89,2%)	103 (86,55%)
CHOLECYSTITIS	9 (11,3%)	2 (5,4%)	11 (9,24%)
CHOLEDOCOLITHIASIS	69 (86,3%)	31 (83,8%)	100 (84,93%)
CBD DILATATION	60 (75%)	31 (83,8%)	91 (76,47%)

Table 14: US findings

- MRCP FINDINGS

In group I, preoperative MRCP was performed in 75 patients and, in GROUP II, it was performed in 23 patients. The following features were analyzed:

	GROUP 1 (N=57)	**GROUP 2 (N=23)**	**TOTAL (n=80)**
CHOLELITHIASIS	54 (94,7%)	23 (100%)	77 (96,25%)
CHOLECYSTITIS	2 (3,5%)	1 (4,3&)	3 (3,75%)
CHOLEDOCOLITHIASIS	57 (100%)	23 (100%)	80 (100%)
CBD DILATATION	47 (82,5%)	23 (100%)	70 (87,5%)

Table 15: MRCP findings

As we see, in some cases, choledocholithiasis was not initially detected with abdominal US, but it was observed in MRCP.

- OTHER DATA

GROUP I:

Laparoscopic CBD stones approach and related complications:

CBDS management	**Group 1 (n=82)**
Transcystic	17 (20,7%)
Choledochotomy	65 (79,3%)

Table 16: CBDS approach

As we can observe, in group 1, removal of choledocholithiasis was performed with LCBDE in 65 patients (79,3%), while transcystic exploration was used in 17 patients (20,7%). When we analyzed the complications rate in these two techniques, we observed that total complications during CBDS clearance presented a higher rate in the choledochotomy approach, but these differences were not statistically significant.

	Transcystic (n=17)	**Choledochotomy (n=65)**	**p value**
Bleeding	1 (5,9%)	1 (1,5%)	NS (0,374)
Infection	0	10 (15,4%)	NS (0,084)
Perforation/phistula	1 (5,9%)	7 10,8%)	NS (0,474)
Pancreatitis	1 (5,9%)	1(1,5%)	NS (0,374)
Total complications	3 (17,64%)	20 (30,76%)	NS (0,497)

Table 17:Complications depending on the CBD approach

Residual choledocholithiasis (RC) rate was analyzed to observe differences depending on the transcystic exploration or CBD exploration, and the following data were found:

	Transcystic (n=17)	**Choledochotomy (n=65)**	**p value**
RC	2 (11,8%)	10 (15,4%)	NS (0,526)

Table 18: RC rates according to CBD approach. RC, residual choledocholithiasis

Kehr drainage was used in 66 patients (80,5%), while in 16 patients (19,5%), it was not inserted.

	Kehr (n=66)	**No Kehr (n=16)**	***p* value**
Bleeding	1 (1,5%)	1 (6,2%)	NS (0,354)
Infection	8 (12,1%)	2 (12,5%)	NS (0,625)
Perforation/phistula	6 (9,1%)	2 (12,5%)	NS (0,489)
Pancreatitis	1 (1,5%)	1 (6,2%)	NS(0,354)
Total complications	16 (24,4%)	6 (37,5%)	NS (0,318)

Table 19: Complications associated with Kehr drain usage

As we see, patients without Kehr drainage presented a higher rate of global complications, but this difference was not statistically significant.

Choledochoscope was used in 78 patients (95,1%), and we analyzed its association with postoperative complications with the following outcomes:

	Choledoscope (n=78)	**No choledoscope (n=4)**	***p* value**
Bleeding	2 (2,6%)	0	NS (0,709)
Infection	9 (11,5%)	1 (25%)	NS (0,412)
Perforation/fistula	7 (9%)	1 (25%)	NS (0,342)
Pancreatitis	2 (2,8%)	0	NS(0,904)
Total complications	20 (25,64%)	2 (50%)	NS (0,318)

Table 20: Choledoscope associated complications

Residual choledocholithiasis rates were analyzed in those interventions where choledoscope was used and those that were performed without it:

	Choledoscope (n=78)	**No choledoscope (n=4)**	***P* value**
RC	12 (15,4%)	0(0.0%)	0,504

Table 21: Choledoscope and RC.

Although not significant, residual choledocholithiasis rates were higher in those patients that underwent LCBDE with choledoscope.

Finally, TransKehr cholangiography was performed in 53 patients (64,6%).

GROUP II:

In group II, all patients underwent ERCP and posterior LC within an average period of 85,06(±72,97) days. The time interval between both procedures has been analyzed by literature and it remains a controversial issue.

- Previous ERCP

In GROUP II, 8 patients (21,62%) required more than one ERCP to clear the CBD. As we previously stated, this outcome is considered a treatment failure.

From all patients that underwent ERCP, resolution was accomplished in 30 patients (81,1%).

Biliar prosthesis was inserted in 10 (12,19%) patients from **GROUP II.** We studied the complications associated with biliar prosthesis insertion.

- Prosthesis associated complications

	Prosthesis(n=10)	**No prosthesis (n=27)**	***p* value**
Bleeding	0	2 (7,7%)	NS (0,516)
Infection	3 (33%)	4 (15,4%)	NS (0,291)
Perforation/fistula	1 (10%)	1 (3,8%)	NS (0,484)
Pancreatitis	1 (10%)	0	NS(0278)
Total complications	5	7	NS (0,119)

Table 22: Biliar prosthesis and complications

As shown in Table 22, no significant difference in terms of complications was observed, although perforation and pancreatitis rates were higher in those patients with biliar prosthesis.

5.2Comparativeanalysis:

- MAIN OUTCOMES

	GROUP 1(n=82)	**GROUP 2**(n=37)	***p*value**
Success	62 (75,6%)	26 (70,3%)	0,345
Complicationsduringcholecystectomy	10 (12,2%)	8 (21,6%)	0,147
Complications during CBD clearance	22 (13,7%)	5 (13,5%)	NS
Bleeding	2 (2,4%)	2 (5,4%)	0,367
Infection	10 (12,2%)	8 (21,6%)	0,147
Perforation/fistula	8 (9,8%)	2 (5,4%)	0,345
Pancreatitis	2(2,4%)	1 (2,7%)	0,667
Residual choledocholithiasis	12 (7,5%)	9 (33,3%)	0,689
Hospitalizationdays	8,76 (media) (7,32-10,19)	6,92 (4,29.9,55)	0,187

Table 23: Outcomes of all patients.

Main results are shown in Table 23. GROUP I had a higher rate of global success than GROUP II, but there was no significant difference. Residual choledocholithiasis appeared in a higher rate among patients from GROUP II, but no statistical difference was observed. GROUP II presented lower average rates of hospitalization, but again this lower rate was notstatiscally significant.

In terms of postoperative complications, no significant difference was observed, but in GROUP II, there was a higher rate of bleeding and infection. Pancreatitis rate was similar between both groups. This is also described by Zhu et al., that observed less

pancreatitis cases in the laparoscopic approach, although bile leak rates were higher than in the endoscopic management [20].

Converted cholecystectomy was performed in 18 patients (15,12%). These conversions were performed because of dense adhesions or unclear anatomy.

Death during hospitalization (1 patient out of 119) was not associated with biliary pathology or the implemented treatment.

6. DISCUSSION

Due to the development of laparoscopic techniques, many centers worldwide have started to perform LCBDE with acceptable results and complications, implicating an alternative for the standard approach, which is nowadays ERCP with ES. Recent large literature reviews and meta-analysis have failed to demonstrate the superiority of one technique compared with others. Nevertheless, it should be said that some cases report lower rates of mortality and shorter hospital stay, as well as lower recurrence rates and number of hospital admissions with one-stage laparoscopic treatment of gallbladder/CBD stones [21].

Our study compared both techniques and showed no significant differences between them regarding success rate of CBD clearance, hospitalization days and intraoperative and postoperative complications, which is comparable to the observed findings in other reported trials.

These outcomes have been evaluated in several studies and meta-analysis. Costi et al (2010) [2]developed a retrospective case-control study comparing the “laparoscopy first” approach in 49 patients versus the “endoscopic first” approach in another 49 patients, showing a higher rate of stones removal in the laparoscopic approach group (86% versus 71%) and no significant difference in terms of complications.

In a meta-analysis carried out by Zhu et al. (2015) [20] that included 8 studies, the CBD clearance rate in the laparoscopic group was higher (90,2% vs 85,7%) than in the endoscopic approach ($p<0,05$), and it also appeared to have shorter hospitalization admissions, while no significance differences were found regarding postoperative morbidity or conversion to other procedures. It concluded that laparoscopic management was more cost-effective and may achieve higher CBDS clearance when in experience hands. This analysis also stated that, since ERCP+ES requires two separate procedures, the patient will require a longer hospitalization and, therefore exposure to risks of anesthesia and sedation is increased.

Our study, by contrast, showed shorter hospitalization admissions in GROUP II, the endoscopicallly managed group.

Bansal et al. (2010)[17]studied 30 patients in a prospective study: 15 of them underwent the laparoscopic approach, and 15 were managed with the endoscopic approach. Success rate was higher in the laparoscopic group (93,5% vs 86,7%), but no significant difference was observed. The rate of complications was similar in both groups. Therefore, our study supports these results, showing equivalent success rate in terms of CBDS clearance and complications, also showing not significant but better results in the laparoscopic group. It was also interesting that Bansal et al. exposed the controversy about the time interval between ERCP and LC, since in a trial carried out by Sgourakis et al. [17] showed that when cholecystectomy was performed within 2

days after ERCP, less conversion rates were observed than in cases where it was performed more than 2 weeks after ERCP (4% vs 31%)

Another similar study was a meta-analysis made by Clayton et al (2006)[22].They analyzed 12 randomized trials with a total of 1357 patient and found no significant difference in successful duct clearance, mortality, total morbidity, major morbidity or need for additional procedures between endoscopic and surgical groups, and concluded that the approach should be adapted to local expertise. However, it pointed out that the laparoscopic management is not yet widely accepted in the USA, and the most common reasons was the longer operating time and lack of equipment.

Similar outcomes were observed in E.A.E.S. multicenter prospective trial, carried out by Cuschieri et al. [23].They compared 150 patients that underwent the laparoscopic approach and another 150 cohort treated with endoscopic approach and no statistical difference was found in terms of ductal stone clearance, as well as in mortality and morbidity. In the laparoscopic group, it is important to highlight that the shortest hospital stay and the lowest postoperative morbidity was observed after transcystic duct exploration. This outcome was also observed in our study (total complications in the transcystic exploration 30,76% vs 17,34% of complications in choledochotomy) , although it was not significant difference. About transcystic-transcholedocal approach, a Cochrane systematic review by Martin et al. [24] concluded that both approaches are safe and effective, although transcholedocal management is associated with an increased risk of bile leaks and requires more expertise in intracorporeal suturing and choledoschopy.

Rogers et al (2010)[25]performed a prospective randomized study with 122 patients comparing both approaches and, once more, observing that they were equivalent in stone clearance efficacy. However, the overall duration of hospitalization was shorter and physician fees lower for the laparoscopic approach.

Sgourakis and Karaliotas published in 2002 a randomized trial with 36 patients that underwent the endoscopic procedure and 42 patients that were treated with the laparoscopic way. Stone detection and clearance rate were equivalent between the groups (24 of 28 stones (86%) cleared by ERCP/ES+LC vs 27 of 32 stones (84%) cleared by LCBDE). In our study, successful outcomes were also equivalent but presented lower rates.

A meta-analysis performed in 2014 by Liu et al. [26] included fifteen studies and concluded that the incidence of bleeding or pancreatitis in the endoscopy group was higher than in the laparoscopic group. Similar outcomes were found in our study, although these differences were very minor. Liu et al. also concluded that the incidence of bile leakage in the endoscopic group was lower. Another important outcome of this study was that the differences in cases of retained stones or total

complications were not statistically different, and, once more, hospitalization stay was shorter than those in the endoscopic group.

Mohamed et al. prospective study (2015) [19]analyzed both techniques in a 150 patient cohort (75 of them in each group), observing a CBD clearance rate of 94,7% in the laparoscopic group and 97% in the endoscopic group. Furthermore, it did not show significant differences between the two groups regarding conversion to the open procedure, hospital stay or postoperative complications.

Cochrane systematic review was done by Dasari et al. in 2013 [27] and it included five trials (n=580), in which 285 patients underwent LCBDE+LC, and 295 patients underwent ERCP+LC. There was no significant difference among two groups in terms of incidence of retained stones (8% vs 11%), mortality (0,7% vs 1%) and morbidity (15% vs 13.5%).

Another aspect that has been analyzed by literature, though not studied in our cohort, is the difference between open CBD exploration and laparoscopic CBD exploration. Our study only included patients that underwent laparoscopic exploration, since it is the most extended procedure in our environment. This is because literature shows that open CBD exploration has proven to imply statistically significantly higher rate of mortality and overall complications compared with patients undergoing the laparoscopic approach. Malawani et al (2017) [28] confirmed this statement in a retrospective cohort study in a total of 2635 patients: open CBDE was associated with a statistically significant increase in mortality, composite morbidity, bleeding, return to the operation room and readmission linked to the first operation. However, retained CBD stones were 2.8 times more likely to appear in the laparoscopic group.

An interesting outcome of this study is the higher rate of residual choledocholithiasis in those patients from GROUP I were choledochoscope was used, since CBD exploration without choledochoscope is strongly correlated to postoperative residual stones and it is highly recommended in LCBDE. Therefore, it might be interesting to analyze if this result is associated to the choledochotomy approach.

Our study has some limitations that should be taken into account. First of all, its retrospective nature. Second, the relatively small number of patients analyzed in each arm of the study. Operative time was not analyzed in this study, but it might have been interesting to compare both techniques, because literature states that increased operative time for laparoscopic CBD clearance may result in increased morbidity [24].Hospital charges were not analyzed either, but several studies have proved that total hospital charges are equivalent between both techniques. Finally, another potential problem of this study is the limited follow-up period of some patients.

7. CONCLUSIONS

Although additional analysis of the long-term follow-up and consequences of either laparoscopic or endoscopic approaches are necessary, this study indicated that the laparoscopic approach of choledocholithiasis is as safe and effective as the gold standard ERCP followed by LC with the nearly same rate of success, hospital stay, and complications and avoids the need for multiple anesthesia sessions and hospital admissions within a short interval.What is more, laparoscopic approach also eliminates the potential risks of ERCP-associated pancreatitis.

It is important to note that, although the laparoscopic technique appears to be equivalent to ERCP and, as literature says, may be more cost effective, it has not been widely accepted by the surgical community.

Given the results of the present study, it seems reasonable to adapt the approach of choledocholithiasis according to local expertise and resources and, having proved their equivalent success rates, we can conclude that the laparoscopic approach is favorable because of the smaller number of procedures and hospital visits.

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9. ABBREVIATIONS

- **BMI:** Body mass index
- **CBD:** Common bile duct
- **CBDS:** Common bile duct stones
- **CT:** Computed tomography
- **EPBD:** Endoscopic papillary balloon dilatation
- **ERCP:**Endoscopic retrograde cholangiopancreatography
- **ES:**Endoscopicsphincterotomy
- **EUS:**Endoscopicultrasound
- **IOC:** Intraoperative cholecystectomy
- **LC:** Laparoscopic cholecystectomy
- **LCBDE**: Laparoscopic common bile duct exploration
- **MRCP:** Magnetic Resonance cholanciopancreatography
- **NOTES:** Natural orifice translumenal endoscopy surgery
- **NS:** Not significant
- **RC:** Residual choledocholithiasis
- **SIL:** Single incision laparoscopy
- **TB**: Total billirubin
- **US:** Ultrasound

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