Endoscopic versus laparoscopic treatment for choledocholithiasis: a prospective randomized controlled trial

Background and study aims: Overall, 5% to 15% of patients undergoing cholecystectomy for cholelithiasis have concomitant bile duct stones, and the incidence of choledocholithiasis increases with age. There is no clear consensus on the best therapeutic approach (endoscopic versus surgical).

Patients and methods: A prospective randomized controlled clinical trial was performed to compare three treatment options for patients with choledocholithiasis at the National Center for Minimally Invasive Surgery in Havana, Cuba from November 2007 to November 2011. The patients were randomized in three groups. Group I: patients who underwent intraoperative cholangiography (IOC) to confirm the choledocholithiasis followed by LC to perform additional procedures [11]. Nevertheless, bile duct stones and their management constitute an important clinical problem. The primary goal in management of choledocholithiasis is to obtain complete clearance of the common duct and cholecystectomy, when indicated [1,2]. Options for management of common bile duct stones (CBDS) are increasing with development of new technologies for diagnosis and treatment. Management of symptomatic or incidentally discovered choledocholithiasis is still controversial. There is no clear consensus on the best therapeutic approach (endoscopic versus surgical) [3–7]. Preoperative endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) are safe and effective options for removing CBDS in most cases, but even when clinical, biochemical, and ultrasound criteria are used, only 10% to 60% of patients will have stones on ERCP. As a result, far too many unnecessary ERCPs are being performed [8]. In fact, one of the best preventive measures to reduce ERCP complications is not to perform it if it is unnecessary.

Introduction ▼

Overall, 5% to 15% of patients undergoing cholecystectomy for cholelithiasis have concomitant bile duct stones, and a small percentage of patients will develop common duct stones after cholecystectomy.[1] Incidence of choledocholithiasis increases with age. About 20% to 25% of patients older than age 60 with symptomatic gallstones have stones in the common bile duct and in the gallbladder [1,2]. Thus, bile duct stones and their management constitute an important clinical problem. The primary goal in management of choledocholithiasis is to obtain complete clearance of the common duct and cholecystectomy, when indicated [1,2]. Options for management of common bile duct stones (CBDS) are increasing with development of new technologies for diagnosis and treatment. Management of symptomatic or incidentally discovered choledocholithiasis is still controversial. There is no clear consensus on the best therapeutic approach (endoscopic versus surgical) [3–7]. Preoperative endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) are safe and effective options for removing CBDS in most cases, but even when clinical, biochemical, and ultrasound criteria are used, only 10% to 60% of patients will have stones on ERCP. As a result, far too many unnecessary ERCPs are being performed [8]. In fact, one of the best preventive measures to reduce ERCP complications is not to perform it if it is unnecessary.

Laparoscopic surgery of CBDS was introduced over 15 years ago and various surgical groups have shown that it has a high success rate [9,10] and is just as efficient and safe as preoperative or postoperative ERCP associated with laparoscopic cholecystectomy (LC), thereby avoiding the need to perform additional procedures [11]. Neverthe-
less, its technical difficulties, long and difficult learning curve and
the need for the allocation of technical resources (high-quality
fluoroscopy and cholangioscopes), which are not available at
many operating theaters, has curtailed its expansion [10].
Use of intraoperative ERCP has slowly increased among various
endoscopic groups, because the transition of ERCP from the
endoscopy unit to the operating room has a short learning curve
(endoscopic groups with expertise in preoperative and post-
operative ERCP) without the high technical requirements needed
by laparoscopic management of the bice duct [12–14].
The aim of this prospective, randomized controlled trial was to
compare the efficacy, safety, and surgical outcomes of the intra-
operative ERCP plus LC (ERCP + LC), preoperative ERCP + LC and la-
paroscopic common bile duct exploration (LCBDE) plus LC
(LCBDE + LC), and determine the most appropriate approach for
patients with choledocholithiasis.

Patients and methods

A prospective, randomized controlled clinical trial was per-
formed to compare 3 treatment options for patients with chole-
docholithiasis. The study was conducted at the National Center
for Minimally Invasive Surgery, Havana, Cuba. This is a tertiary
referral university-affiliated center specializing in endoscopic
and laparoscopic surgery (Multidisciplinary work group). All
the procedures were performed by the 5 authors who are very ex-
perienced in both ERCP and laparoscopy. Surgical and endoscopic
techniques were standardized before starting the protocol; 2 ex-
pierenced biliary endoscopists (J. R. T, R. B. Q) performed all ERCP
in both groups of patients, while 3 experienced laparoscopic sur-
geons (J. E. B. G, R. T. P, M. A. M. A) performed LC and LCBDE. The
protocol for anesthesia was the same in all patients.
Informed consent was obtained from patients before study partic-
tipation. The study was approved by our Institution Ethical Com-
mittee and by The Cuban Public Registry of Clinical Trials (Unique
ID number: RPCECO0000013). The trial was performed in com-
pance with the Helsinki Declaration and ICH-GCP (efficacy sec-
tion).
The sample size calculation is as follows: With 3 groups and a bi-
nary endpoint (success-failure), we constructed a 3×2 contin-
tency table. We used the Grizzle, Starmer, and Koch method [15].
The hypotheses tested were:
\[
\begin{align*}
H_0 & : \pi_1 = \pi_2 = \pi_3 \\
H_1 & : \pi_1 \neq \pi_2 \neq \pi_3
\end{align*}
\]
Here \(\pi_1, \pi_2, \pi_3\) are the expected success rates in each population
group. We employed information from Rochon’s paper [16], that
is, \(p^{\ast}[n_1 (1-n_1) n_2 (1-n_2) n_3 (1-n_3)]\) outcomes vector; \(\phi(p^{\ast}) =
[n_1 n_2 n_3]\) (subset of measures of interest); \(X=\text{Identity matrix of}
order 3\) (design matrix);
\[
C = \begin{bmatrix} 1 & 1 & 1 \\ 0 & -1 & -1
\end{bmatrix}; \ h = 0. \ Substitution produced the following formula:
\[
\lambda_0 = \frac{n \left[ (1-n_1)(1-n_2) \left( \frac{1}{2} \right) + n_1 \left( 1-n_2 \right) \left( \frac{1}{2} \right) + n_2 \left( 1-n_1 \right) \left( \frac{1}{2} \right) + n_1 n_2 \left( \frac{1}{2} \right) \right] \left( \frac{1}{2} \right) + n_1 \left( 1-n_2 \right) \left( \frac{1}{2} \right) + n_2 \left( 1-n_1 \right) \left( \frac{1}{2} \right) + n_1 n_2 \left( \frac{1}{2} \right) \right] \left( \frac{1}{2} \right) + n_1 \left( 1-n_2 \right) \left( \frac{1}{2} \right) + n_2 \left( 1-n_1 \right) \left( \frac{1}{2} \right) + n_1 n_2 \left( \frac{1}{2} \right) \right] \left( \frac{1}{2} \right) + n_1 \left( 1-n_2 \right) \left( \frac{1}{2} \right) + n_2 \left( 1-n_1 \right) \left( \frac{1}{2} \right) + n_1 n_2 \left( \frac{1}{2} \right) \right] \left( \frac{1}{2} \right) + n_1 \left( 1-n_2 \right) \left( \frac{1}{2} \right) + n_2 \left( 1-n_1 \right) \left( \frac{1}{2} \right) + n_1 n_2 \left( \frac{1}{2} \right) \right] \left( \frac{1}{2} \right) + n_1 \left( 1-n_2 \right) \left( \frac{1}{2} \right) + n_2 \left( 1-n_1 \right) \left( \frac{1}{2} \right) + n_1 n_2 \left( \frac{1}{2} \right) \right] \left( \frac{1}{2} \right)
\]
where \(\lambda_0\) is the non-centrality parameter of the non-central \(\chi_2^2\)
that satisfies the area lying to the right of the critical point \(\chi_2^{2.1-\alpha}\)
is the desired power 1-\(\beta\) for the design, and where \(\chi_2^{2.1-\alpha}\) repre-
sents the 1-\(\alpha\) percentil of the central \(\chi_2^2\) with 2 degrees of free-
dom (the number of degrees of freedom is the number of rows
of the matrix \(C\); \(\alpha\) is the significance level of the test); \(n\) repre-
sents the sample size in each of the three treatment groups.
We chose the values: \(\alpha=0.05, \beta=0.2, \pi_1=0.85, \pi_2=0.8, \pi_3=0.94\).
We get \(\lambda_0=9.635, n=90\). Assuming a possible 10% of missing
data due to protocol violations, we concluded that we should in-
clude 100 patients per group, for a total of 300 patients.
The primary endpoint was the rate of success in clearing ductal
stones. From November 2007 to November 2011, 404 patients with
suspected CBDS admitted to the hospital were evaluated prospec-
tively for study eligibility. The intake was restricted to appropri-
ate patients [American Society of Anesthesiologists (ASA) I, II and
III] in whom choledocholithiasis was suspected on the basis of
clinical features (biliary colic with jaundice and recent acute pan-
creatitis), liver function tests (elevated bilirubin, alkaline phos-
phatase, gamma-glutamyltranspeptidase), and external ultra-
sound findings (showing possible CBDS or a dilated common bile
duct >8 mm).
Further exclusion criteria included cholangitis or pancreatitis,
age < 18 years, ASA IV and V, suspected common bile duct (CBD)
malignancy, previous cholecystectomy, previous ERCP and/or ES,
and contraindications to ERCP or laparoscopic surgery. Moreover,
patients treated with total or partial gastric resection were ex-
cluded.
After obtaining consent, eligible patients were randomized in 3
treatment groups using computer-generated random number se-
quences in concealed envelopes with block randomization de-
sign.
Group I patients underwent intraoperative cholangiography
(IOC) to confirm choledocholithiasis followed by LC associated
with intraoperative ERCP, ES and endoscopic stone extraction
(ESE). All patients were placed in the usual supine position for
LC. LC with IOC was always attempted and images were obtained
during this step. ERCP and ES were performed during LC. The sur-
geon carried out LC without completely dissecting the gallblad-
der from its bed. This maneuver facilitated ending LC after ERCP,
because bowel distention during this procedure limits gallblad-
der dissection. Besides, in case of ERCP failure, traction of the ve-
sicular bottom facilitated CBD visualization.
We performed a “rendezvous” technique only in those patients,
in which endoscopic cannulation of the papilla was difficult
(when the papilla is hidden within a diverticulum). We used a
guided wire through the cystic duct into the CBD to facilitate bile
duct cannulation at subsequent endoscopy.
Group II patients underwent preoperative ERCP, ES with ESE fol-
lowed by LC (24 to 48 hours later). All patients were placed in
prone position.
Group III underwent IOC to confirm the choledocholithiasis fol-
lowed by LC associated with LCBDE and laparoscopic stone ex-
traction. We performed LCBDE via trans cystic, choledochotomy
and a few patients underwent flexible cholangioscopy. First,
we performed transcystic common bile duct exploration but if a
patient had an anomalous anatomy, proximal stones and large or
numerous stones, we used choledochotomy for common bile
duct exploration. LCBDE via choledochotomy required placement
of a T-tube and drain.
We did not use magnetic resonance cholangiopancreatography
(MRCP) in our institution.
The following criteria were recorded: success rates (ERCP cannu-
lation rate and surgical success rate), success rates of ductal stone
clearance, conversion rates, morbidity (complications were de-
defined as any intraoperative or postoperative (30 days) event that
altered the clinical course such as complications of ERCP including pancreatitis, perforation and bleeding. CBD retained stones, mortality (postoperative mortality was defined as death within 30 days of surgery), total operative time in minutes, and length of hospital stay.

The level of power for the study was set at 80% with a 5% significance level. Categorical variables were compared by x² test, with Yates correction and the Fisher exact test (two-tailed) when necessary. Continuous variables were compared by the Student t-test or HSD Tukey, depending on distribution. All P values were two-sided. P<0.05 indicated a statistically significant difference. Data were analyzed on an intention-to-treat basis. All calculations were performed by using SPSS_ version 21.0.

Results

A total of 404 patients with suspected choledocholithiasis were admitted to the National Center for Minimally Invasive Surgery of the Havana Medical University, from November 2007 to November 2011. After excluding 104 ineligible cases (acute cholecystitis, cholangitis, pancreatitis and suspected CBD malignancy), 300 patients were included in the trial and randomized to either group I (Intraoperative ERCP/ES) (n = 99), group II (Preoperative ERCP/ES) (n = 101), or group III (LCBDE) (n = 100). Seven patients had protocol violations (management different from that dictated by random allocation) and 2 had anesthesia complications. As a result, a total of 134 patients were diagnosed with presence of choledocholithiasis and treated during the study period (Fig. 1).

Table 1 shows the preoperative variables (age, CBD diameter, stone size and stone number) of the three groups.

The success rate for ductal stone clearance in each group was approximately the same. The success rate for stone clearance in the Intraoperative ERCP/ES group (97.8%) was higher than in the Preoperative ERCP/ES group (93.3%) and similar in the LCBDE group (97.7%). There were no significant differences among the groups (Table 2).

Postoperative complications occurred in 6 patients (13.3%) in the preoperative ERCP/ES group; 5 with cholecystitis and 1 with pancreatitis due to ERCP/ES. In the LCBDE group, postoperative complications occurred in 2 patients (4.7%); these patients had bile leak from CBD closure and were treated conservatively with broad-spectrum antibiotics. No postoperative complications were reported in the intraoperative ERCP/ES group. Postoperative complications lasted for a significantly shorter time in the intraoperative ERCP/ES group than in the preoperative ERCP/ES group (P<0.012) (Table 3).

Retained stones occurred in 1 patient (2.2%) in the intraoperative ERCP/ES group and 1 patient (2.3%) in the LCBDE group and were treated with postoperative ERCP. In the preoperative ERCP/ES group, retained stones occurred in 5 patients (11.1%) and were treated with postoperative ERCP. The rate of retained stones was significantly lower in the intraoperative ERCP/ES and LCBDE groups than in the preoperative ERCP/ES group. There were no significant differences among the groups (Table 4).

Mean operative time was 94.2 minutes (45–300), 9.8 minutes (30–240) and 117 minutes (40–270) for groups I, II and III respectively. Mean duration of the ERCP/ES procedure for groups I and II was 24.7 minutes and 25 minutes, respectively. These
times were significantly shorter than for LCBDE group III (49.7 minutes) \( (P<0.001) \).

There were no deaths or cases of conversion to open surgery. Length of hospital stay was significantly shorter in the intraoperative ERCP/ES group (mean 1.2 days) than in the preoperative ERCP/ES group (mean 3.1 days) \( (P<0.0001) \) and LCBDE group (mean 2.1 days) \( (P<0.012) \).

**Discussion**

Over the past 20 years, LC has become the gold standard for surgical treatment of symptomatic biliary lithiasis, and its development has favored the appearance of a group of new endoscopic/surgical therapeutic possibilities for patients with choledocholithiasis, namely total laparoscopic treatment of choledocholithiasis versus endoscopic treatment using intraoperative ERCP (both single-stage treatments), or preoperative ERCP and postoperative ERCP with LC (2-stage treatment) [6].

Very few studies are available comparing single-stage treatments (LCBDE and intraoperative ERCP) and 2-stage treatment (preoperative ERCP) [6]. Since the introduction of laparoscopic choledochectomy in our institution in 1993, the standard treatment for CBDs had been preoperative ERCP/ES, followed by LC and postoperative ERCP/ES. With the advance in technology and laparoscopic techniques, we started to perform LCBDE (1995) and intraoperative ERCP/ES (2003), and this randomized trial compares the results among the 3 preoperative approaches. The preoperative and noninvasive tests for predicting CBDs such as clinical examination, history, laboratory tests and ultrasound have a high negative predictive value (92%–99%). However, the positive predictive value is less satisfactory, and in patients with high suspicion of choledocholithiasis, this is only shown in 13% to 58% of cases. Application of these criteria reveals a high rate of false-positive diagnoses and many unnecessary ERCPs (40%–50%) [17]. Currently MRCP and endoscopic ultrasound are used routinely before ERCP to prevent unnecessary procedures but they are not available in our institution [5–11,18]. IOC failure occurred at a rate (8%) which is similar to other publications. The single most frequent reason for failure to complete IOC in our series was an inability to cannulate the cystic duct. The success of ERCP cannulation in our study is comparable to that reported in the literature for patients with CBDs [19,20].

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**Table 2** Success rates of ductal stone clearance of the three groups.

<table>
<thead>
<tr>
<th>Diagnosis and treatment of choledocholithiasis</th>
<th>Group</th>
<th>ERCP/ES</th>
<th>Preoperative ERCP/ES</th>
<th>LCBDE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I: Intraoperative ERCP/ES n = 99</td>
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<tr>
<td>Group II: Preoperative ERCP/ES n = 101</td>
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<tr>
<td>Group III: LCBDE n = 100</td>
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</table>

<table>
<thead>
<tr>
<th>Positive for choledocholithiasis</th>
<th>Group</th>
<th>ERCP/ES</th>
<th>Preoperative ERCP/ES</th>
<th>LCBDE</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 46</td>
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<tr>
<td>n = 45</td>
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<td>n = 43</td>
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<tbody>
<tr>
<td>45 (97.8%)</td>
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<tr>
<td>42 (93.3%)</td>
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<tr>
<td>42 (97.7%)</td>
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**Table 3** Postoperative complications.

<table>
<thead>
<tr>
<th>Postoperative complication</th>
<th>Group</th>
<th>ERCP/ES</th>
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<th>LCBDE</th>
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<td></td>
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<tr>
<td>Group III: LCBDE n = 100</td>
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<th>Preoperative ERCP/ES</th>
<th>LCBDE</th>
</tr>
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<tbody>
<tr>
<td>0 (0%)</td>
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<tr>
<td>6 (13.3%)</td>
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<tr>
<td>2 (4.7%)</td>
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**Table 4** Retained stones.

<table>
<thead>
<tr>
<th>Retained stones</th>
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<th>ERCP/ES</th>
<th>Preoperative ERCP/ES</th>
<th>LCBDE</th>
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<tbody>
<tr>
<td>Group I: Intraoperative ERCP/ES n = 99</td>
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<tr>
<td>Group II: Preoperative ERCP/ES n = 101</td>
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<td></td>
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<tr>
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<th>ERCP/ES</th>
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<th>LCBDE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (2.2%)</td>
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<td></td>
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<tr>
<td>5 (11.1%)</td>
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<tr>
<td>1 (2.3%)</td>
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</table>

**Table 5** Comparison of surgical results among the three groups.

<table>
<thead>
<tr>
<th>Comparison of surgical results among the three groups</th>
<th>Groups</th>
<th>RR</th>
<th>CI</th>
<th>X&lt;sup&gt;2&lt;/sup&gt;</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I Versus Group II</td>
<td></td>
<td>1.05</td>
<td>0.96–1.5</td>
<td>1.08</td>
<td>(&lt;0.36)</td>
</tr>
<tr>
<td>Group I Versus Group III</td>
<td></td>
<td>1.00</td>
<td>0.94–1.07</td>
<td>0.45</td>
<td>(1.00)</td>
</tr>
<tr>
<td>Group III Versus Group II</td>
<td></td>
<td>1.05</td>
<td>0.96–1.15</td>
<td>0.44</td>
<td>(&lt;0.61)</td>
</tr>
</tbody>
</table>

**Table 6** Comparison of surgical results among the three groups.

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<tr>
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<th>RR</th>
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<th>X&lt;sup&gt;2&lt;/sup&gt;</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I Versus Group II</td>
<td></td>
<td>0.00</td>
<td>0.00–0.86</td>
<td>14.48</td>
<td>1.00</td>
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<tr>
<td>Group I Versus Group III</td>
<td></td>
<td>0.00</td>
<td>0.00–3.84</td>
<td>11.02</td>
<td>1.00</td>
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<tr>
<td>Group III Versus Group II</td>
<td></td>
<td>0.35</td>
<td>0.07–1.63</td>
<td>0.04</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**Table 7** Comparison of surgical results among the three groups.

<table>
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<tr>
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<tr>
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</table>

ERCP/ES, endoscopic retrograde cholangiopancreatography plus endoscopic sphincterotomy; LCBDE, laparoscopic common bile duct exploration

1 Relative risk
2 Confidence Intervals
to bowel insufflations) and the technique’s limitations were related to impacted CBD stones, so we omitted this step in most cases in the clinical trial, as had ElGeidie et al. [28], because the endoscopist and team were very experienced with ERCP (more than 10,000 ERCP).

Single-stage treatments facilitate performance of LC simultaneously. Recurrent biliary complications are more common in patients who do not have elective cholecystectomy after management of cholecodolithiasis by ES [28,29]. When there is a time lag between ERCP/ES and LC, some patients may develop cholecystitis (5–22%) [30–32]. That difference can be partially explained by the length of the interval between the 2 procedures, which is not well defined, as even in the multicenter trial by the European Association for Endoscopic Surgery (EAES) the interval between endoscopic papillosphincterotomy and LC was not specified [33]. Patients awaiting LC are known to have a high rate of readmission and complications due to acute cholecystitis, pancreatitis, empyema, and cholangitis; others showed that in case of delayed cholecystectomy, performed over 2 weeks after ES, there is a higher conversion rate, increasing from 4% when LC was done within 2 weeks, to 31% between 2 and 6 weeks, and 16% after 6 weeks [34]. Therefore, elective cholecystectomy is indicated 24 to 48 hours after clearance of CBD. Nevertheless, some authors report that it is no possible to know whether the acute inflammation is due to pre-ERCP acute cholecystitis or whether it is induced by ERCP [28].

In our study, a significant amount of local inflammation was found in 5 patients and was associated with pain. We consider that clinically relevant because residual local inflammation in patients after ERCP may negatively affect operative outcomes and necessitate a longer hospital stay. Studies have shown that presence of inflammation as an independent risk factor for bile duct injury during LC [35].

At the time of laparoscopic surgery, bile duct stones can be removed with a straightforward transcyelic approach or with technically demanding cholecystectomy. LCBDE in all candidates offers advantages over preoperative ERCP/ES: equivalent removal of duct stones with fewer procedures, lower cost, and preservation of the biliary sphincter. When laparoscopic bile duct exploration is used, the operation is longer. Consequently, in elderly patients and those with significant comorbidity who may not tolerate longer procedures, the advantage may be lost [36].

Several trials have compared clinical outcomes with the 2-stage approach to those with a single-stage strategy. Rogers and colleagues [36] randomized 122 patients to LC plus LCBDE or to ERCP/ES plus LC. Although the techniques had equivalent efficacy and safety, length of hospitalization was 2 days shorter for those who underwent the combined laparoscopic procedure. Recently, Lu and colleagues [38] performed a meta-analysis of 9 randomized trials that compared 2-stage ERCP and LC with combined LC and bile duct exploration. In 787 patients, the approaches were found to have equivalent efficacy and safety. The longer hospital stay seen in the ERCP group in the individual trials was not evident; however, significantly more procedures were required in the ERCP group than in the combined laparoscopic group. The problem with applicability of these data, however, is that most surgeons are not trained to perform LCBDE. Bin Wang and colleagues [39] concluded that with regard to stone clearance and overall complication rates, preoperative ERCP is equal to intraoperative ERCP in patients with gallbladder and common bile duct stones. However, intraoperative ERCP is associated with a reduced incidence of ERCP-related pancreatitis and results in a shorter hospital stay. The total hospital stay was significantly shorter with intraoperative ERCP than with preoperative ERCP (RR 2.22, 95% CI 1.98–2.46; P < 0.01). A longer hospital stay was required for preoperative ERCP as a result of management of complications and organization of scheduling slots for preoperative ERCP and LC. Also residual local inflammation in patients after ERCP may negatively affect operative outcomes and demand more length of hospital stay.

Use of intraoperative ERCP has slowly increased among various endoscopic groups [12–14]. La Greca et al. [14] reviewed all published studies on intraoperative ERCP and found 27 original papers that included between 8 and 96 patients each, thus analyzing a total of 795 patients. The success rate ranged between 69.2% and 100% and averaged 92.3%. The average duration of intraoperative endoscopy was 35 minutes and the average duration of surgery was 104 minutes. The average conversion rate to open surgery was 4.7% and morbidity was 5.1% (0–19%). Mortality is extremely rare, and from the 27 publications reviewed, only 3 patient deaths were reported, giving rise to a total mortality rate of 0.37%.

The 3 types of treatment are effective and the choice of approach depends on a patient’s particular circumstances and on the experience of the different endoscopic and surgical teams at each center [10].

Conclusions

We conclude that intraoperative ERCP/ES for choledocholithiasis results in a higher rate of choledocholithiasis clearance, shorter hospital stay, and lower morbidity, but further research with a larger study population is necessary to determine the procedure’s additional benefits. Results to date suggests that in appropriate patients, single-stage treatments are the best options.

Competing interests: None

References


11 Martin DJ, Vernon DR, Toouli J. Surgical versus endoscopic treatment of bile duct stones. Cochrane Database Syst Rev 2006; CD003327
16 Rochon J. The application of the GSK method to the determination of minimum sample sizes. Biometrics 1989; 45: 193–205
22 Guda NM, Freeman ML. 30 years of ERCP and still the same problems? Endoscopy 2007; 39: 833–835
24 Petersen BT. Combined approaches to endoscopic retrograde biliary access after failed transpapillary approach. Gastrointest Endosc 2007; 5: 136–140
31 Mallory JS, Baron TH, Dominitz JA. Compilations of ERCP. Gastrointest Endosc 2002; 57: 633–638
32 Yasui T, Takahata Sh, Kono H et al. Is cholecystectomy necessary after endoscopic treatment of bile duct stones in patients older than 80 years of age? J Gastroenterol 2012; 47: 65–70
34 Byrne MF, McLoughlin MT, Mitchell RM et al. The fate of patients who undergo “preoperative” ERCP to clear known or suspected bile duct stones. Surg Endosc 2009; 23: 74–79