Diagnostic accuracy of intraoperative cholangiography for detection of anatomical variations of the biliary system

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Introduction
Intraoperative cholangiography (IOC) during laparoscopic cholecystectomy (LC) is valuable in the detection of biliary abnormalities. In this study, we aimed to investigate the diagnostic accuracy of IOC during LC for the detection of anatomic variations of the biliary system, as well as the visualization ability of IOC on determining the normal anatomy of the biliary tree.

Patients and methods
A total of 56 patients, admitted with symptomatic gall stones, who met our inclusion criteria were involved in this prospective randomized study.
LCs with cholangiograms were performed by a laparoscopic surgeon and reviewed by a radiologist and were carried out by using a standard four-cannula technique.

Results
Overall, 68% of patients were females, and their mean age was 42±10 years. There were 21 patients known to have different chronic illnesses, including hypertension (14%), diabetes mellitus (12%), chronic liver disease (7%), and ischemic heart disease (4%). Regarding the results of preoperative ultrasound, approximately two-thirds of patients had normal ultrasound, whereas the other one-third had dilated intrahepatic biliary duct (13%) and common bile duct sludge (16%). Residency was statistically significant with presence of stones (P=0.007). Visualization ability of IOC achieved 100% visualization rate for the whole 54 cases that underwent IOC. Failure rate of IOC was 4%, and failure was attributed mainly owing to technical errors or narrowing of cystic duct in two cases per each.

Conclusion
The results of the current study encourage using IOC as an effective, accurate, feasible, and safe technique to visualize the biliary tree while performing LC.

Keywords:
diagnostic accuracy, intraoperative cholangiography, laparoscopic cholecystectomy

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Introduction

Nowadays, laparoscopic cholecystectomy (LC) has grown to replace open surgery and become the gold standard procedure for symptomatic gall stones and cholecystitis since its clinical introduction ∼25 years ago [1,2]. LC is a selective procedure that is considered as one of the most commonly performed surgical procedures worldwide [3]. It was reported that ∼90 000 LC operations were performed annually in Canada [4], 750 000 in the United States [5], 66 000 in the United Kingdom [6], and 60 000 in Japan [7]. Bile duct injury (BDI) is a rare complication, with an estimated incidence of 0.7% [8]. However, it is a very serious complication of LC, which significantly affects the quality of life and overall survival [9]. Despite this increasing number of performed procedures, the BDI rates have not declined. The initial learning curve can no longer justify the ongoing injury rates that eventually require multiple procedures and extensive reconstructive surgery. Many patients have frequently repeated and extended hospitalizations, leading to substantial long-term morbidity and increased cost of health care [10]. Therefore, there is an urgent need to overcome this serious complication.

Intraoperative cholangiography (IOC) during LC is valuable in the detection of common bile duct (CBD) stones, the delineation of bile duct anatomy, the facilitation of dissection, the prevention of biliary tract injuries, and the identification of other abnormalities such as fistulas, cysts, and biliary system tumors [11,12]. BDI could be prevented if cholangiography is done through the cystic behavior before any structure is transected [13]. However, this technique also showed some limitations; therefore, there is a large debate regarding using it as a routine or a selective procedure. Many researchers suggested that IOC should be done always in situations where the anatomy is not clear, as it cannot always prevent choledochotomy but can decrease the rate of BDI [12,14]. Moreover, it can be used in patients with a history of jaundice, a palpable common duct stone, multiple small stones in the gallbladder, and gallstone pancreatitis [15]. Routine cholangiography increases the cost of the procedure and the cost of an uncomplicated LC when comparing with selective cholangiography [13]. In this study, we aimed to investigate the diagnostic accuracy of IOC during LC for the detection of anatomic variations of the biliary system, as well as the visualization ability of IOC on determining the normal anatomy of the biliary tree.

Patients and methods

Study design and patients

This is a prospective randomized study that was carried out at the Department of Surgery, Faculty of Medicine, Suez Canal University, between June 2017 and February 2019. We enrolled patients admitted with symptomatic gall stones, within the age range of 18–60 years old and whose general condition was acceptable for anesthesia. We excluded patients with previous upper abdominal surgery, pregnancy, hypersensitivity to the contrast used, impaired kidney function, chronic liver disease, bleeding diathesis, and CBD stones referred for preoperative endoscopic retrograde cholangiopancreatography (ERCP). Approval from institutional review board was obtained before starting the fieldwork. An informed consent was obtained from all participants after informing them of the procedure's risk and the chances for conversion to open surgery.

Data collection

All patients of the study were subjected to preoperative assessment during which we collected data on demographics, symptoms, comorbid conditions, and current history of pancreatitis or cholangitis. Patients presenting with acute cholangitis or pancreatitis were allowed to settle first before the operation. Preoperative ERCP with or without sphincterotomy was performed before LC in those patients presenting with jaundice, abnormal liver function tests, or unresolved cholangitis. We then performed local abdominal examination for detection of organomegaly, palpable abdominal masses, positive Murphy's sign, and signs of cholangitis. The following preoperative investigations were performed: complete blood count, international normalized ratio, liver function tests, serum bilirubin, and renal function tests. We also performed abdominal ultrasound for dilated CBD and intrahepatic biliary radical dilatation.

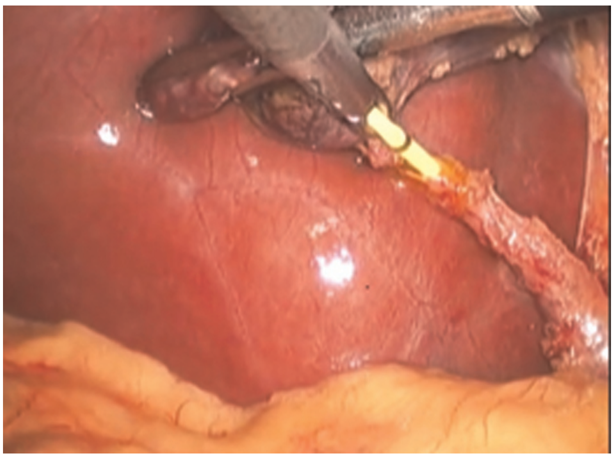
Operative management

General anesthesia was given to all participants. The patients were placed in supine position. LC with cholangiography was carried out using a standard four-cannula technique. Traction of the gallbladder fundus was applied in a cephalic direction with a grasper placed through the midclavicular port. IOC was performed using either the following:

(1) A cholangiogram catheter or a ureteric catheter (5 Fr): the cystic duct was identified and dissected free, clipped proximally to prevent spillage of gallbladder content, then incised along one-half of its circumference just distal to the previously placed titanium clip. Then, a catheter was guided into the partially transected proximal cystic duct (using a guide wire when necessary) (Fig. 1) and was secured in place in the cystic duct with a cholangioclamp.
(2) A specialized grasper with the cholangio needle catheter used to inject 5–15 ml of contrast material to visualize the biliary ductal system. A photograph was taken of the cystic duct cholangiogram. After cholangiography, the biliary duct was flushed with saline. The catheter was removed, two clips placed on the common duct end of the cystic duct, and it was divided with scissors.

Advancement of the C-Arm (Phillips BV Pulsera mobile C-arm, Royal Phillips Company, USA) was done to the table, and then after proper positioning, an iodinated contrast agent Urografin 30% 15 ml was injected through the catheter, then anteroposterior and oblique views were taken. This allows the biliary tree to be envisioned under fluorescent scan (Figs 2 and 3).

Figure 1

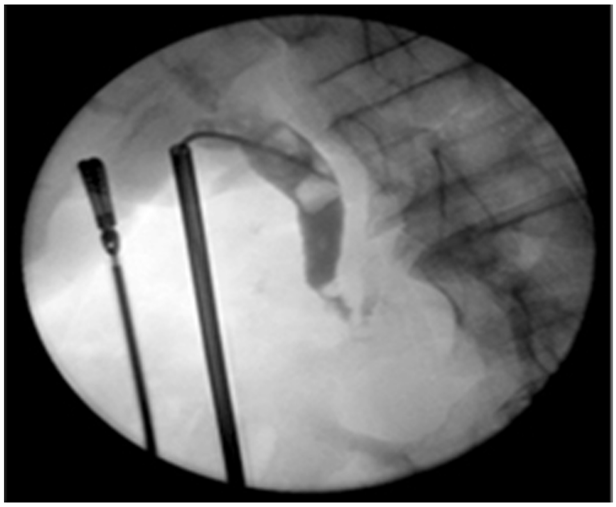


A catheter was guided into the partially transected proximal cystic duct.

Figure 2

IOC with complete filling of the biliary tree, normal tapering of the lower CBD, and contrast flowing into duodenum. CBD, common bile duct; IOC, intraoperative cholangiography.

Figure 3



IOC initial image showing CBD stones as there is a filling defect within the CBD and failure of dye to reach the duodenum. CBD, common bile duct; IOC, intraoperative cholangiography.

Discharge and follow-up

Patients were allowed to go home when fully comfortable, fully mobile, and tolerating normal diet. Clinical improvement was defined as a reduction of abdominal pain and tenderness, normalization of laboratory values, and neutral fluid balance. Oral diet was reintroduced gradually. Following discharge, patients were followed up clinically (abdominal pain, guarding, masses) every 2 weeks for the first month, and then every month for 3 months and radiologically (abdominal ultrasound) if indicated. Follow-up was continued for 6 months to detect late postoperative complications.

Outcome measures

The visualization ability of IOC was determined based on the frequency and rate of recognition of the normal anatomy of the biliary tree, anatomical variations, and biliary abnormalities. Feasibility was assessed based on the success rate of IOC and operation time. Accuracy was estimated by sensitivity, specificity, positive predictive value, and negative predictive value of IOC to detect biliary abnormalities.

Statistical analysis

All statistical analyses were performed using the statistical package for the social sciences (SPSS), version 22. Descriptive statistics were applied in numerical form (mean, SD, or percentages) to describe the quantitative variables. Diagrammatic and tabular forms were used to describe the qualitative variables. Associations between variables were tested for significance using χ^2 test for categorical variables and t test for continuous variables with normally distributed data. Nonnormally distributed data were tested using Fisher's exact for categorical variables and Mann–Whitney U tests for continuous variables. Diagnostic accuracy was assessed through estimation of sensitivity, specificity, positive predictive value, and negative predictive value. A two sided P values less than 0.05 were considered statistically significant.

Results

Baseline characteristics

In the current study, we included 56 patients. Most of them were females (68%), with a mean age of 42±10 years. Subgroup analysis revealed a statistically significant difference between both sexes regarding age distribution (P=0.03). Most patients were nonsmokers (86%). A total of 21 patients had associated chronic illnesses (Table 1). Approximately, 91% of patients had elective LC. The indications for LC included acute calculous cholecystitis and chronic calculous cholecystitis with history of pancreatitis, but the majority of patients had LC for chronic calculous cholecystitis. More than three-fourths of the patients had normal liver function test results and normal total leukocytic count (TLC). Regarding the results of preoperative ultrasound, approximately two-thirds of patients had normal ultrasound, whereas the other one-third had dilated intrahepatic biliary duct (IHBD) (13%) and CBD sludge (16%). Baseline characteristics are detailed in Table 2.

Association between stone and demographic characteristics

We found no significant association between age, sex (yet females were more likely to have stones), comorbid chronic illnesses, as well as all laboratory parameters (liver function tests and TLC), with the presence of

Table 1 Demographic characteristics of the patients

Parameters	*n* (%)
Age (years) (mean±SD)	42±10
Sex	
Male	18 (32)
Female	38 (68)
Residency	
Urban	29 (52)
Rural	27 (48)
Smoking	8 (14)
Special habits 'addict'	1 (2)
Chronic diseases	
Hypertension	8 (14)
DM	7 (12)
Chronic liver disease	4 (7)
IHD	2 (4)
Indication of LC	
Acute calculous cholecystitis	5 (9)
Chronic calculous cholecystitis	46 (82)
Chronic calculous cholecystitis with history of pancreatitis	5 (9)
Type of surgery	
Elective	51 (91)
Emergency	5 (9)
Laboratory parameters	
High AST	13 (23)
High ALT	13 (23)
High ALP	1 (2)
High total bilirubin	5 (9)
High TLC	5 (9)

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; DM, diabetes mellitus; IHD, ischemic heart disease; LC, laparoscopic cholecystectomy; TLC, total leukocytic count.

Table 2 Preoperative radiological data

Findings	*n* (%)
Normal biliary tree	35 (62)
Stones in CBD	0
Dilated IHBD	7 (13)
Dilated CBD	17 (30)
CBD sludge	9 (16)
Filling defect	0 (0)
CBD diameter (mm) (mean±SD)	7±1

CBD, common bile duct; IHBD, intrahepatic biliary duct.

CBD stones during LC. Interestingly, all patients who had stones were from rural areas (*P*=0.007). Concerning the ultrasound findings, it was found that stones' carriers were more likely to have abnormal ultrasound, dilated CBD, dilated IHBD, and bile duct sludge than those without stones. However, the only statistically significant association was between CBD dilatation status and presence of stones (*P*=0.04) (Table 3).

Intraoperative cholangiography visualization ability

We could successfully visualize the whole biliary tree including IHBDs and extrahepatic biliary ducts (cystic duct, hepatic duct, common hepatic duct, CBD, and ampulla of Vater) achieving a 100% visualization rate for the whole 54 cases who underwent IOC (Table 4).

We identified 13 anatomical variations including low cystic duct insertion (seven), a medial cystic duct insertion (two), barrel cystic duct course (one), and both aberrant and accessory bile ducts (three). Concerning the anatomical sites where the stones where found, there were only six cases who had stones. All of these stones were in extrahepatic bile ducts specifically in the cystic duct (three) and the CBD (three). A total of 13 patients had anatomical variations (24%). The commonest of them were low cystic duct insertion (*N*=7) followed by the presence of aberrant and accessory bile ducts (*N*=3), then medial duct insertion (*N*=2), and then barrel cystic duct course (*N*=1). The failure rate of IOC was 4% (two patients) and failure was attributed mainly owing to technical errors (one case) or narrowing of cystic duct (one case).

Associations between preoperative ultrasound findings and IOC findings revealed that the majority of patients with positive IOC findings had a CBD less than 10 mm and associated with presence of CBD sludge. Associations between preoperative laboratory data and

Table 3 Association between patients' characteristics and presence of common bile duct stones during laparoscopic cholecystectomy

Parameters	Stones [*n* (%)]	*P*
Age (years)		
<50	3 (50)	0.13
≥50	3 (50)	
Sex		
Males	2 (33)	0.94
Females	4 (67)	
Residency		
Urban	0	0.007*
Rural	6 (100)	
Chronic diseases		
Hypertension	1 (17)	0.86
DM	0	0.32
Chronic liver disease	1 (17)	0.33
IHD	0	0.61
Laboratory parameters		
AST		
Normal	4 (67)	0.53
High	2 (33)	
ALT		
Normal	4 (67)	0.53
High	2 (33)	
ALP		
Normal	6 (100)	0.72
High	0	
Total bilirubin		
Normal	5 (83)	0.48
High	1 (17)	
TLC		
Normal	6 (100)	0.41
High	0	
Anatomic findings		
Normal biliary tree		
No	4 (67)	0.11
Yes	2 (33)	
Dilated CBD		
No	2 (33)	0.04*
Yes	4 (67)	
Dilated IHBD		
No	5 (83)	0.74
Yes	1 (17)	
Bile duct sludge		
No	4 (67)	0.42
Yes	2 (33)	

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; CBD, common bile duct; DM, diabetes mellitus; IHBD, intrahepatic biliary duct; IHD, ischemic heart disease; TLC, total leukocytic count. **P* values less than 0.05 indicate statistical significance.

IOC findings revealed that the majority of patients with positive IOC findings had liver function tests (Table 5).

The mean operative time including both the time of IOC and LC was 75±20 min. During LC, six cases were found to have stones and one with dilated bile duct without stones (Table 6).

Table 4 Visualization ability of intraoperative cholangiography

Variables	*n* (%)
Intrahepatic bile ducts	54 (100)
Extrahepatic bile ducts	
Cystic duct	54 (100)
Hepatic ducts and confluence	54 (100)
Common hepatic duct	54 (100)
Common bile duct	54 (100)
Ampulla of Vater	54 (100)

Table 5 Findings of intraoperative cholangiography

Variables	*n* (%)
Anatomic variations	13 (24)
Low cystic duct insertion	7 (13)
A medial cystic duct insertion	2 (4)
Barrel cystic duct course	1 (2)
Both aberrant and accessory bile ducts	3 (5)
Sites of stones	
CBD	3 (5)
Cystic duct	3 (5)

CBD, common bile duct.

Table 6 Intraoperative details

Variables	*n* (%)
Operative time (min) (mean±SD)	75±20
Intraoperative findings	
Normal biliary tree	49 (87)
Single symptomatic ductal stone	1 (2)
Asymptomatic ductal stones	5 (9)
Dilated bile duct without stones	1 (2)

Predictors of bile duct stones during intraoperative cholangiography

Sensitivity of the preoperative laboratory data for prediction of positive IOC was variable. The highest sensitivity of the abnormal values was high aspartate transaminase (AST) and high alanine transaminase (ALT), followed by high bilirubin. Among abnormal preoperative ultrasound findings, dilated CBD had the highest sensitivity, followed by bile duct sludge, and then dilated IHBD. Accuracy of eight variables was tested as predictors of bile duct stones. The majority of these variables were more specific rather than sensitive, including age older than 50 years, high liver function tests [AST, ALT, alkaline phosphatase (ALP), and total bilirubin], and dilated CBD. The only predictor with higher sensitivity was female sex (Table 7 and Figs 4 and 5).

Discussion

The goal of the current prospective randomized study was to assess the feasibility, accuracy, and visualization ability of IOC in delineating the biliary tree and detection of anatomical and pathological abnormalities. We found that IOC successfully identified all structures of the biliary tree in 54/56 patients (success rate: 96%). IOC was accurate in detection of biliary stones with high sensitivity and specificity (100%). The usage of IOC during LC was associated with a high visualization rate, 100% sensitivity and specificity, and 96% success rate.

Visualization ability

In our study, IOC successfully identified all structures of the biliary tree in 54 patients. In former studies, the IOC visualization rates of the cystic duct, common hepatic duct, cystic-hepatic ducts junction, and CBD were 71.4–100, 33.3–100, 25–100, and 50–100%, respectively [16]. We identified thirteen anatomical variations, including low cystic duct insertion (seven), a medial cystic duct insertion (two), barrel cystic duct course (one), and both aberrant and accessory bile ducts (three). Further, only six cases had stones: distal cystic duct (three) and CBD (three). These variations in the visualization ability of IOC are attributed to many factors such as the patients' position, the contrast material itself, and the surgeons experience [16,17].

Table 7 Predictors of bile duct stones in intraoperative cholangiography

Predictors	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Age >50	50	78	21	93
Female sex	67	32	10	89
High AST	33	78	15	90
High ALT	33	78	15	90
High ALP	0	98	0	98
High total bilirubin	16	92	20	90
High TLC	0	90	0	88
Dilated CBD	67	73	23	94

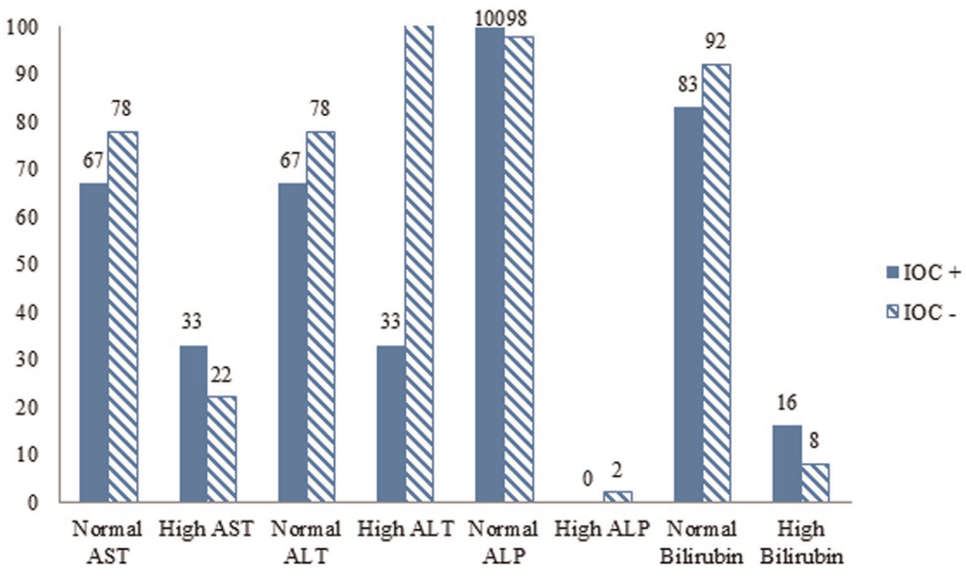
ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; CBD, common bile duct; NPV, negative predictive value; PPV, positive predictive value; TLC, total leukocytic count.

The high visualization ability of IOC is considered an advantage that counterweighs its invasiveness. Moreover, it surpasses other modalities such as ultrasound which cannot detect all biliary structures [18]. Laparoscopic ultrasound can sometimes achieve 100% visualization rate; however, it has some limitations. First, it is highly dependent on the operator's experience [19]. Second, it is associated with a learning curve during initial use [20]. Third, it is inefficient in differentiating the anatomical variations of the bile duct. Last but not least, it cannot determine the flow of bile into the duodenum [21]. Magnetic resonance cholangiopancreatography (MRCP) and ERCP are also highly sensitive and specific tools, yet both have significant drawbacks. The former cannot visualize small stones and the latter can be associated with post-ERCP pancreatitis, duodenal perforation, cholangitis, and gastrointestinal hemorrhage [21].

Accuracy

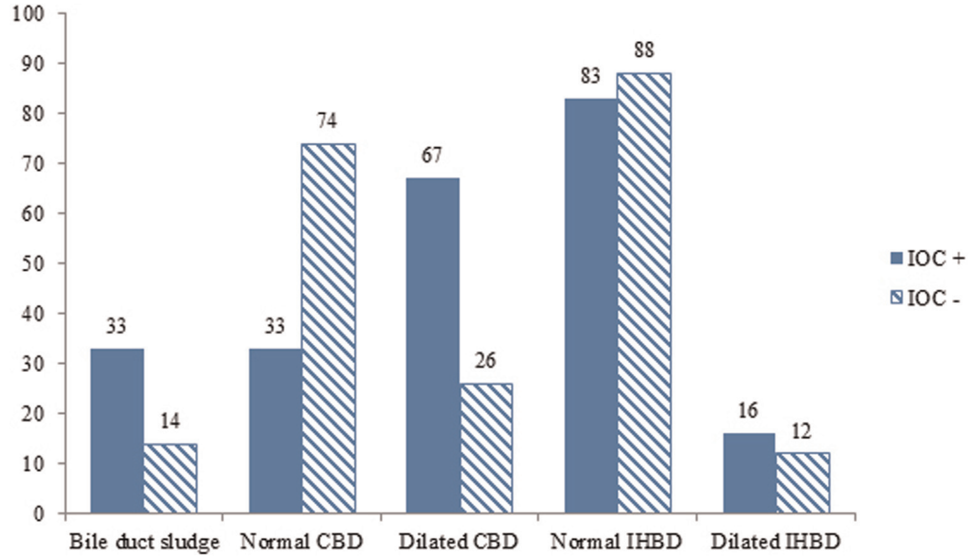
The current study revealed high sensitivity and specificity (100%) for IOC in detection of biliary stones. In agreement, Videhult *et al.* [22] found that the sensitivity of IOC for CBD stones detection is 97%, whereas the specificity is 99%. Similarly, Hope *et al.* [16] reported high accuracy rates in stone

Figure 4



Preoperative biochemical predictive factors of IOC. IOC, intraoperative cholangiography.

Figure 5



Preoperative radiological predictors of IOC. IOC, intraoperative cholangiography.

detection that ranged from 92.2 to 99%. Ultrasound is able to detect CBD dilatation; albeit, its role is limited regarding the detection of CBD stones with a low sensitivity of 23–65% [23]. However, intraoperative ultrasound sensitivity ranges between 96 and 100%, whereas specificity ranges between 99 and 100% [21]. As mentioned earlier, intraoperative ultrasound is extremely reliant on the operator's performance. Both MRCP and ERCP have high (up to 100%) accuracy rates for detection of CBD stones. For instance, the sensitivity of MRCP ranges between 81 and 100% and the specificity ranges between 73 and 100%, whereas the sensitivity of ERCP ranges between 84 and 97% and the specificity ranges between 87 and 100% [24].

Feasibility

In our study, IOC was successful in 96% of the cases; it failed only due to technical errors in one case, and because of narrow cystic duct in another case. According to previous studies, the success rate of IOC ranges from 92 to 97% [25–27]. Failure may occur owing to narrowing of the cystic duct, adhesions in Calot's triangle, or difficulties in the dissection of the cystic duct [21].

The success rate of IOC is similar to that of laparoscopic ultrasound. Perry *et al.* [28] reported a success rate of 95.5% for laparoscopic ultrasound in detecting CBD stones. However, it has poor visualization rates; it can detect bile duct dilatation, yet not CBD stones. Moreover, ultrasound is affected by patient-related factors and examiner's experience [23]. One of the common reasons of IOC feasibility is the real-time visualization, which saves the time and cost of preoperative evaluation [29], unlike other modalities which require patient preparation, such as ultrasound and MRCP [23].

The operative duration in the current study was 75 ±20 min. In comparison, Verma *et al.* [30] found that the operative duration without IOC was 90 min, and with IOC, was 118 min. The variability is probably attributed to the type of IOC, whether it is selective or routine. Researchers found that routine IOC saves the wasted time in calling a radiologist and instrument preparation during selective IOC [30]. Comparing the feasibility of IOC with other modalities such as ERCP and MRCP favor's the former. In addition to time consumption, there is the hazardous burden of post-ERCP complications and the high costs of MRCP, yet without significant reductions in morbidity rate. From an economic perspective, the cost of IOC is estimated to be around US$720. With an estimate of 0.5% incidence of BDI, routine IOC would cost more than US$370 000 to prevent one case of BDI [31]. Therefore, selective IOC is a more appealing idea in low socioeconomic countries, to save the financial cost, the relatively prolonged surgery, the needed instruments, radiation exposure, and the risk of false-positive results [28].

To perform selective IOC, surgeons have to rely on preoperative predictive factors to determine which cases should be evaluated with IOC. Therefore, we studied the value of preoperative laboratory and radiological data in the prediction of biliary disease for those undergoing LC. Regarding laboratory tests, elevated ALP had the highest specificity, followed by elevated bilirubin, then high TLC and lastly AST and ALT; however, they all had low sensitivity. Of the ultrasound findings, dilated CBD had the highest sensitivity and specificity in the prediction of biliary duct stones (66 and 73%, respectively). This is in agreement with Photi *et al.* [32] but with slight variations; of the laboratory tests, bilirubin had the highest specificity, followed by ALP, and then ALT (89.2, 82.3, and 78.1%, respectively). Similarly, these tests had low-to-moderate sensitivity (33.6, 51, and 51%, respectively). However, ultrasound findings had high specificity and moderate sensitivity (84 vs. 45.2%, respectively).

Strengths and limitations

The study investigated multiple outcomes that are of concern to all surgeons about using IOC during LC, including the visualization ability, reliability, feasibility, and associated morbidity and mortality. However, the study had some limitations, including the small sample size and absence of a comparison group. Yet, the comprehensiveness and thorough investigative efforts exerted in the present study outweigh those limitations.

Recommendations

Surgeons should (a) consider using IOC during LC for better intraoperative visualization and to improve postoperative outcomes, (b) be trained to perform IOC during LC to save time and achieve the best outcomes, and (c) consider IOC during LC for selective cases based on predictive factors such as high bilirubin, ALP, ALT, and AST. Further studies are required to determine more accurate predictive factors of positive IOC findings to facilitate selection of patient for IOC.

Conclusions

The results of the current study encourage using IOC as an effective, accurate, feasible, and safe technique to visualize the biliary tree while performing LC. In spite of the highly optimistic results, there are some drawbacks to be considered including the additional demand of time, money, human resources, and staff training. Therefore, in low-income settings, selective IOC based on preoperative laboratory and radiological predictors is recommended. These predictors include high bilirubin, high ALP, high ALT, and dilated CBD. Of notice, these predictors are characterized by high specificity with low sensitivity, which qualifies them as rule-out tests for selection for IOC during LC.

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Conflicts of interest

There are no conflicts of interest.

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