"COMPARISON OF LAPAROSCOPIC CHOLECYSTECTOMY WITH AND WITHOUT THE USE OF INDOCYANINE GREEN DYE A 1 YEAR OBSERVATIONAL COHORT STUDY AT A TERTIARY HOSPITAL IN BELAGAVI"

BY

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Dissertation

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Sub: Institutional Ethical Clearance for the study.

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LIST OF ABBREVATIONS		
SI No	**ABBREVATIONS**	**FULL FORM**
1	ICG	INDOCYANINE GREEN
2	CBD	COMMON BILE DUCT
3	CHD	COMMON HEPATIC DUCT
4	CVS	CRITICAL VIEW OF SAFETY
5	BDI	BILE DUCT INJURY
6	IOC	INTRAOPERATIVE CHOLANGIOGRAPHY
7	CCC	CHOLECYSTOCHOLANGIOGRAPHY
8	LUS	LAPAROSCOPIC ULTRASOUND
9	NIRF-C	NEAR INFRARED FLUORESENCE CHOLANGIOGRAPHY
10	NIR	NEAR INFRARED
11	LC	LAPAROSCOPIC CHOLECYSTECTOMIES
12	KLE	KARNATAKA LINGAYAT EDUCATION
13	IV	INTRAVENOUS

14	ALP	ALKALINE PHOSPHATASE
15	SGOT	SERUM GLUTAMIC OXALOACETIC TRANSAMINASE
16	SGPT	SERUM GLUTAMIC PYRUVIC TRANSAMINASE

ABSTRACT

Gall stone disease is one of the most common pathologies encountered in surgical wards these days, With 10-15% of the general population suffering from symptomatic or asymptomatic cholelithiasis, which makes it one of the most common pathologies of gall bladder and biliary tree. Laparoscopic cholecystectomy is currently considered as the gold standard treatment for the same. However with the increase in laparoscopic cholecystectomies the incidence of bile duct injuries has also increased. Various factors like adhesions, altered biliary anatomy and edematous biliary anatomy can lead to BDI. In this study laparoscopic cholecystectomies were performed with and without the use of Indocyanine Green dye. The aim of this study was to know the effectiveness of ICG in clearly delineating the biliary anatomy and determine the perioperative complication rates.

2.5mg of ICG dye was given 1 hour 30minutes to 2 hours preoperatively. A total of 68 cases were included in this study with 50% of them performed with the use of ICG dye.

The time taken to identify the critical view of safety(CVS) and the identification rates of cystic duct, common bile duct and common hepatic duct were calculated.

It was observed that of the two groups the CVS was achieved significantly faster with a mean time of 24.2 minutes in the ICG group whereas 36.7 minutes in the control group. The overall time for surgery was also significantly better in ICG group with a mean time of 58.4mins.

Similarly identification rates of Cystic duct, CBD and CHD were much higher in ICG group with identification rates of 82%, 67% and 55% respectively. The

identification of CBD was significantly better with ICG as compared to that without ICG, with a p value of 0.05.

No significant difference was seen between the postoperative complications, length of hospital stay and rates of conversion to open.

Thus this study concluded that laparoscopic cholecystectomies with the use of ICG dye have a better overall surgical outcome with significantly better identification of the biliary anatomy.

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INTRODUCTION

Gall stone disease is one of the most common pathologies encountered in surgical wards these days, With 10-15%(1) of the general population suffering from symptomatic or asymptomatic cholelithiasis, which makes it one of the most common pathologies of gall bladder and biliary tree. In Patients suffering from asymptomatic cholelithiasis, it was recently discovered that the risk of developing symptoms or complications is 1-2% per year with 20% of them developing a symptomatic disease at a 15-year follow-up.

Moreover, cholelithiasis can further lead to various other complications which include cholecystitis, cholangitis, choledocholithiasis, gallstone pancreatitis, and rarely cholangiocarcinoma. (2)

The etiology of gall stones is extensive and multifactorial ranging from various, genetic, dietary, anatomical, metabolic, and pathological factors(3).

Various treatment modalities have been employed for the treatment of cholelithiasis, with cholecystectomy being the standard line of treatment for the same.

The most prevalent form of cholecystectomy and the gold standard treatment is laparoscopic cholecystectomy(1). Overall the incidence of cholelithiasis is on the rise, and the overall rates of laparoscopic cholecystectomies are rising rapidly. Day care laparoscopic cholecystectomies are considered a safe modality of treatment(4)

However, the escalation in cholecystectomies and the transition from an open to laparoscopic approach have correlated with a concomitant rise in bile duct injuries(5)

Frequent and substantial variations, typically ranging from 30% to 40% are frequently observed in the anatomical configuration of the biliary tree. (6,7) Furthermore, the formation of adhesions in and around the calot's triangle due to diverse factors is a well-documented phenomenon (8)

These factors give rise to complexities in the precise intraoperative delineation of biliary anatomy, representing a prevalent challenge encountered by surgeons during laparoscopic cholecystectomy. These variations and difficulties in identifying the biliary anatomy increase the possibility of dreaded complications like bile duct injury and post-operative bile leak etc(5) An innovative technique for visualizing the anatomy of the biliary tree during laparoscopic cholecystectomy is with the use of ICG dye (9). The purpose of this study is to determine whether laparoscopic cholecystectomy with the use of ICG dye fluroscopy can effectively visualize "the anatomy of the biliary tree.

AIMS AND OBJECTIVES

1. To determine the effectiveness of ICG dye in visualization of the cystic duct, hepatic duct and common bile duct and to evaluate whether early identification of the critical view of safety can be obtained by using" ICG fluoroscopy.
2. To assess the rate of peri-operative complications with and without the use of ICG fluoroscopy.

REVIEW OF LITERATURE

A. Embryology

A hepatic diverticulum begins to develop from the primitive foregut's ventral wall during the fourth week of life. The cranial, as well as caudal buds from the hepatic diverticulum, become apparent by the end of the fourth week. The liver lobes and a portion of the extrahepatic biliary tree originate from the cranial bud. Both superior and inferior buds emerge from the caudal buds.

The gall bladder and cystic duct originate from the superior caudal bud, whereas the left and right ventral pancreas originate from the inferior caudal bud.

1**. 3-mm stage**: Cranial bud which blossoms into liver lobes. The gallbladder and extrahepatic biliary system develop from the caudal bud. By day 26 of development, the cystic diverticulum develops from the caudal duct which forms the gall bladder and cystic duct by the end of 4 weeks.

2**. 5mm stage**: A common hepatic duct is formed from part of pars hepatica distal to the origin of pars cystica and a common bile duct (CBD) is formed from a part between pars cystica and duodenal part of foregut.

3. **7mm stage**: The liver, gallbladder, hepatic ducts, cystic duct, and ventral pancreas form.

4. **12-mm stage**: It is not until “the sixth or seventh week of gestation that the ventral pancreatic bud has completed a rotation of 180 degrees clockwise around the duodenum. This rotation causes the ventral and dorsal buds to” fuse together, resulting in the formation of the entire pancreas.

B. Surgical Anatomy

1. GALL BLADDER

- 7 to 10cm long, pear-shaped
- Within the gallbladder fossa, which is situated on the inferior surface of the liver.
- Average capacity is 30 to 50ml (Maximum 300ml in cases of outflow obstruction)(10)

The gall bladder is anatomically divided into 4 parts –

a) **Fundus**: Round in shape with a blind end exceeding 2 cm below the inferior margin of the liver

b) **Body**: Composed of elastic tissue which helps in distension.

c) **Infundibulum**: It is a mucosal outpouching present at the junction of the cystic duct & neck

d) **Neck**: Situated at the lowest point of the gall bladder fossa that connects to the cystic duct.

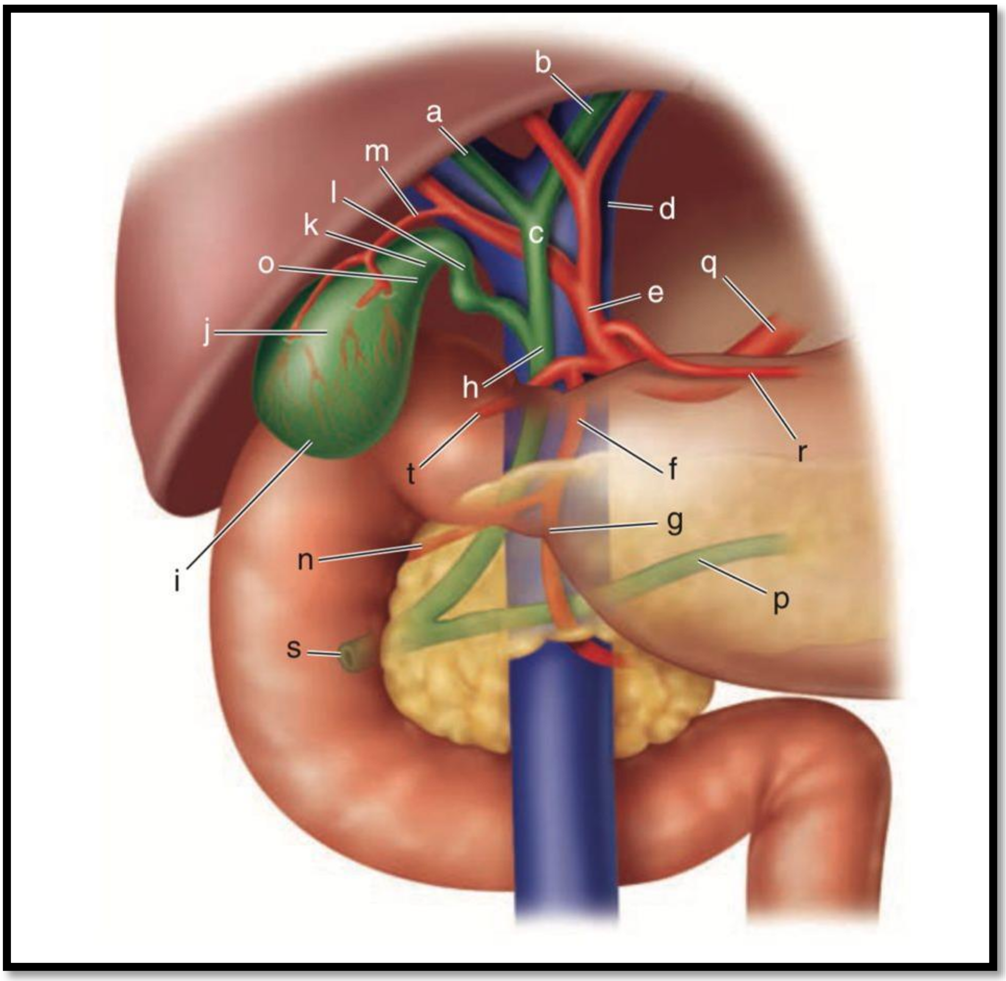


Image 1: Anatomy of Gallbladder

a. Right “hepatic duct
b. Left hepatic duct
c. Common hepatic duct
d. Portal vein
e. Proper hepatic artery
f. Gastroduodenal artery
g. Right gastroepiploic
h. Common bile duct
i. Fundus of gall bladder
j. Body of gall bladder
k. Infundibulum of gall bladder
l. Cystic duct
m. Cystic artery
n. Superior pancreaticoduodenal artery
o. Neck of” gall bladder
p. Pancreatic duct

2. EXTRAHEPATIC BILIARY TREE

a. **Hepatic ducts**: Left hepatic duct is longer than right, although right dilates more. The liver is where both hepatic ducts end.

b. **Common hepatic duct**: The common hepatic duct (CHD) is formed when the right and left hepatic ducts converge close to the liver's surface. With a diameter of 4mm, the length ranges from 1 to 4 cm.

Resides to the right of the hepatic artery and ahead of the portal vein.

c. **Cystic duct**: It exits from the gall bladder. Has variable length and course. It has spirally arranged folds in mucosa known as valves of Heister.

d. **Common bile duct**: When the cystic duct acutely enters the main hepatic duct, the CBD is created. 7 to 11cm in length, & 5 to 10mm in diameter(11)

i. **Supraduodenal**: This 2.5cm-long anatomical feature is located on the right side of the hepatic artery, prior to the portal vein, and along the lesser omentum's free border.

ii. **The retroduodenal** segment lies posterior to the initial part of the duodenum and extends away from the portal vein and hepatic artery.

iii. **The infraduodenal** segment is on the posterior surface of the pancreatic head & traverses through it.

iv. **The intraduodenal** segment joins with the pancreatic duct and ends by opening to the ampulla of Vater in 2nd part of the duodenum.(11)

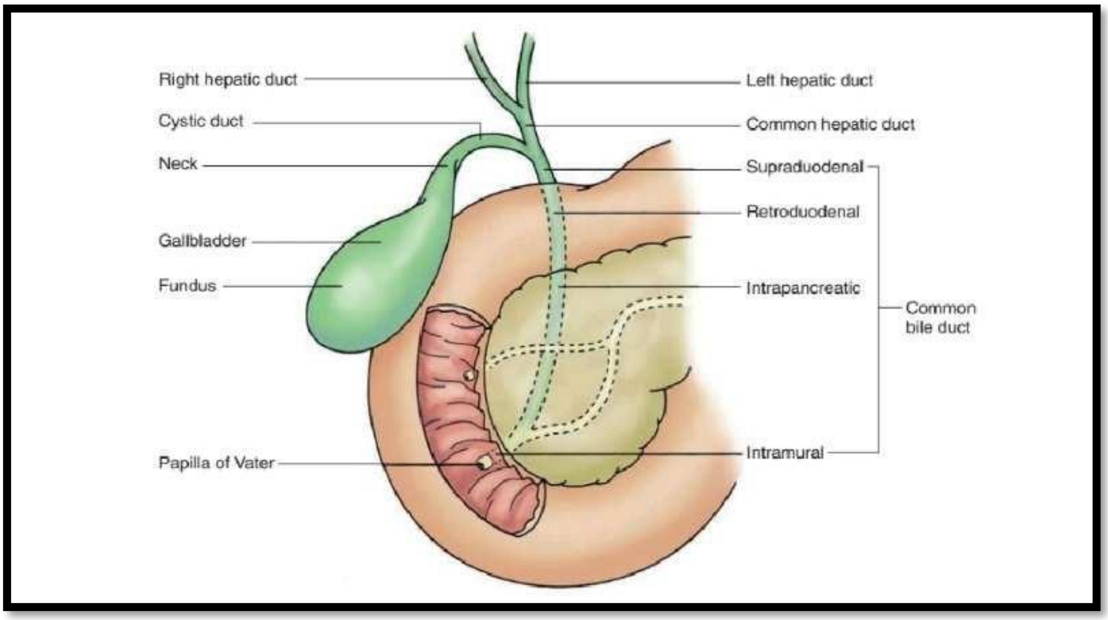


Image 2: Anatomy of Common Bile Duct

3. BLOOD SUPPLY

A. ARTERIAL SUPPLY :

- A cystic artery has a variable origin
- It originates as a branch of the right hepatic artery (located close to the cystic duct in Calot's triangle) that nourishes the gall bladder.
- At the gallbladder's neck, it produces shallow and deep branches that anastomose over the fundus and body of the gallbladder.

Caterpillar turn / Moynihan's hump: dangerous anomaly comprising of short cystic artery and tortuous right hepatic artery which can lead to inadvertent arterial injury or bleeding during cholecystectomy (11)

B. **VENOUS DRAINAGE:**

- The right portal vein carries several minor veins that tributary into the liver from the gallbladder bed.
- Veins draining the bile ducts drain into 9 o'clock & 3 o'clock veins along the common biliary channel(12)

C. **LYMPHATICS:**

The cystic lymph node of Lund, which is situated at the angle where the cystic and common hepatic ducts join, drains the gall bladder. Subsequently, the efferent vessels empty into the celiac lymph nodes and the liver at its hilum. The subserosal lymphatic vessels of the gallbladder and the subcapsular lymphatic vessels of the liver combine (12)

4. ANATOMICAL VARIATIONS :

The classical description of the biliary tree appears only in $1/3^{rd}$ of the patients (11)

Anatomical variations seen in,

A. Gall bladder

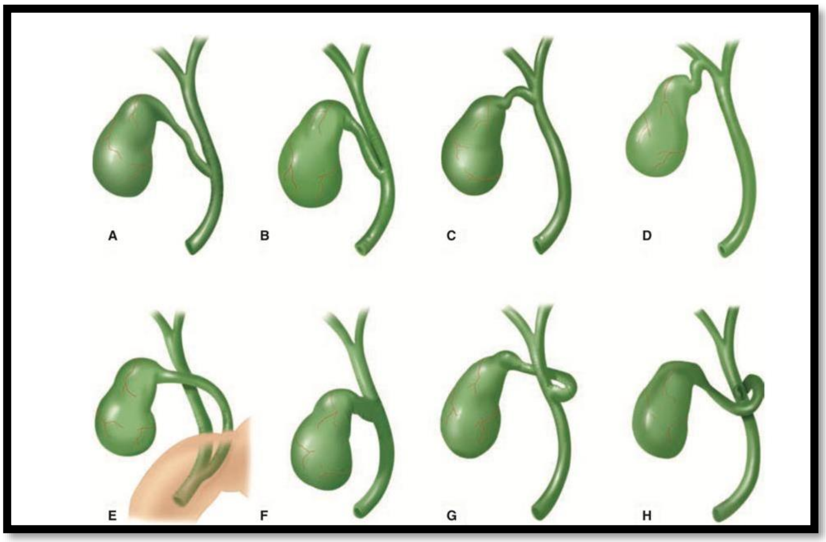
- Intrahepatic
- Rudimentary
- Duplication
- Left sided gallbladder
- Retro displaced gallbladder
- Floating gallbladder

B. Cystic duct

- The low point where the CHD and cystic duct converge
- Adherent cystic duct to CHD
- High point where the common and cystic hepatic ducts converge
- The right hepatic duct receives a cystic duct drainage.
- The lengthy cystic duct joins the CHD after the duodenum.
- Absence of cystic duct
- The cystic duct enters the CHD anteriorly after crossing it posteriorly.
- The CHD and the cystic duct connect posteriorly. (11)

Furthermore, the luschka auxiliary ducts may empty straight into the liver fossa or any other location along the biliary tree from the gall bladder's body.

About 5% of people have accessory right hepatic ducts. (11,13)

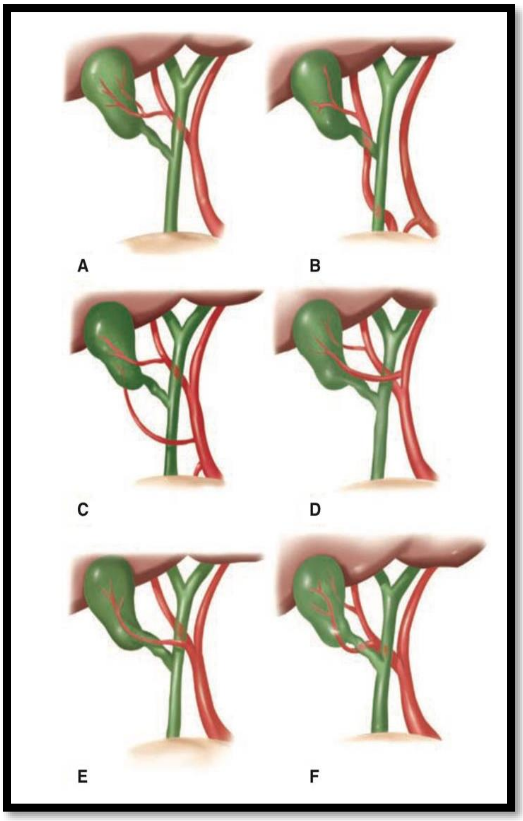


(11)

Image 3: Anatomical variations of Cystic Duct

C. Hepatic and cystic artery

As many as 40–50% of cases are associated with anomalies in the hepatic and cystic arteries.



A. Cystic “artery from right hepatic artery
B. Accessory cystic artery/ replaced cystic artery arising from superior mesenteric artery (10%)
C. Two cystic artery from right and common hepatic artery
D. Two cystic artery from right and left hepatic artery
E. Cystic artery running anterior to common hepatic duct
F. Dual cystic artery from right hepatic” artery

Image 4: Anatomical variation of Cystic Artery

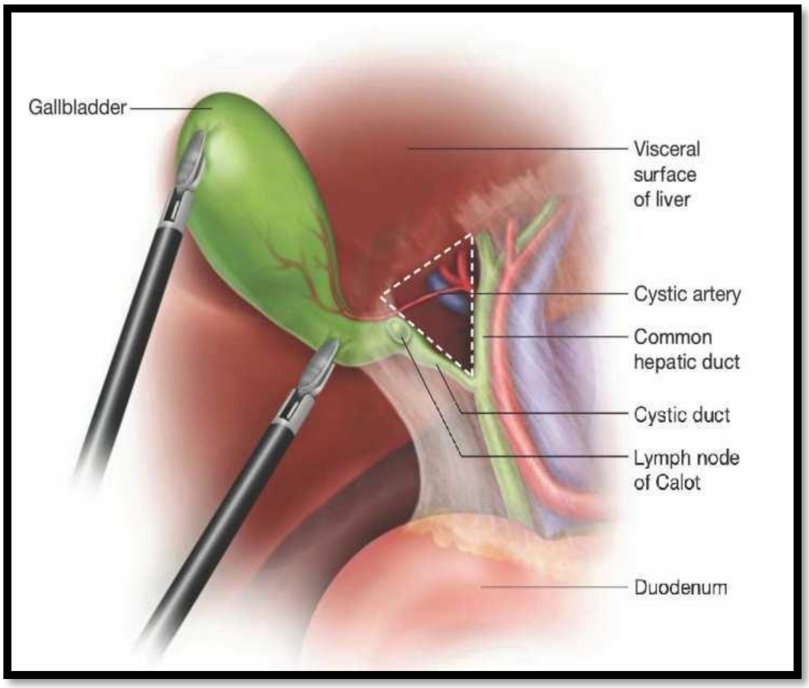
5. CALOT’S “TRIANGLE :

BOUNDARIES:

- Superiorly- cystic artery
- Medially: common hepatic duct
- Laterally: cystic duct and the gallbladder's neck

CALOT'S TRIANGLE CONTENTS

1. Cystic lymph node of Lund
2. Small cystic veins
3. Autonomic nerves" piercing gall bladder
4. Adipose tissue
5. Right hepatic artery (tortious)
6. Some accessory ducts draining GB. (14)



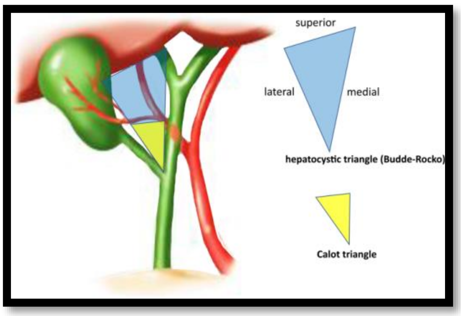


Image 5: Anatomy of Calots Triangle

6. CHOLECYSTOHEPATIC TRIANGLE

BOUNDARIES:

- Superiorly- the inferior surface of the liver
- Medially: common hepatic duct
- Laterally: cystic duct and the neck of gall bladder (15)

7. LAPAROSCOPIC ANATOMY OF GALL BLADDER

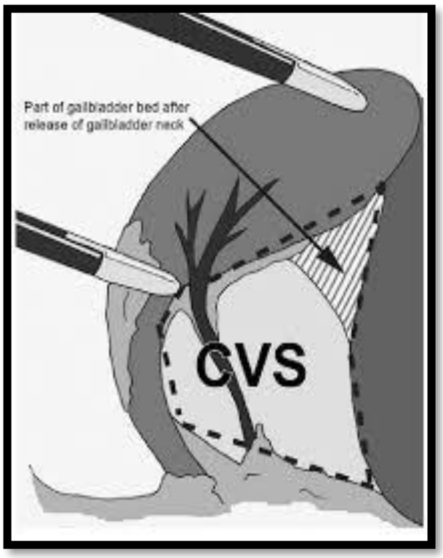
During a laparoscopic cholecystectomy, the cystic duct and cystic artery can be located utilizing the Critical View of Safety (CVS) method. **(16)**

Standards to attain Critical View of Safety (CVS)

a. The hepatocystic triangle loses both fat and fibrous tissue. The hepatocystic triangle" is formed by the liver's border, CHD, and cystic duct. (Note- There's no need to expose CHD and CBD.)

b. Lower gallbladder removal from liver exposes cystic plate. Gall bladder fossa contains the liver bed, or cystic plate.

Only who structures must be visible entering the gall bladder(17)



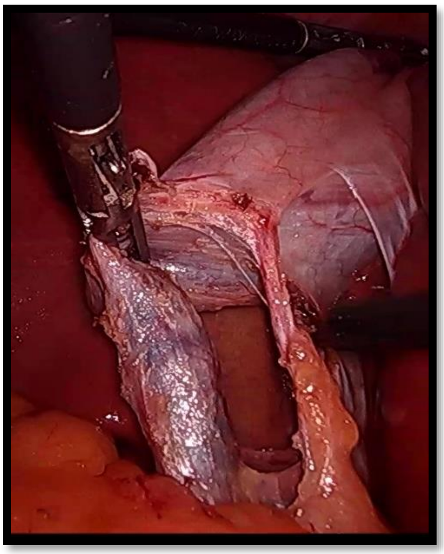


Image 6: Critical View of safety

Rouviere's sulcus-

It is a fissure or sulcus that most people can easily perceive between the liver's right and caudate lobes. This is located at the level of the porta hepatis, where the right pedicle penetrates the liver. To avoid injuring the bile duct, the dissection should be carried out above this sulcus. (18)

C. LAPAROSCOPIC CHOLECYSTECTOMY

Steps of Laparoscopic Cholecystectomy

1. **Anesthesia**: General anesthesia is administered for all laparoscopic cholecystectomy procedures.

2. **Patient Positioning**: With their arms by their sides and their feet tightly strapped, the patient is positioned in a supine position.

3. **Preparation**: After intubation, a Foley catheter and a Ryle's tube are inserted.

4. **Creating Pneumoperitoneum**: A pneumoperitoneum is established to create a working space in the peritoneal cavity, maintained at a pressure of 12-14 mmHg. There are two techniques to achieve this:

    1. **Closed (Veres Needle) Technique**:

        - At the umbilicus, a Veres needle is introduced through the anterior abdominal wall.

- The position is confirmed using normal saline with a plunger-less syringe.
- CO_2 is insufflated at a rate of 2 liters per minute.
- Correct intra-abdominal placement is confirmed by observing uniform abdominal distension.

2. **Open (Hasson) Technique**:

   - An incision is made supraumbilically, and layers are opened under direct vision to enter the peritoneum.
   - A 10mm trocar is inserted and secured with sutures.
   - Further CO_2 insufflation is performed

5. **Placement of Ports and Adequate Exposure:** A port measuring 10 mm is placed in the periumbilical area. The abdominal cavity, including the gall bladder, omentum, liver, colon, and pelvis, is examined with a 30-degree laparoscope to check for adhesions or other diseases. One additional 10mm port and two, 5mm ports are strategically placed within direct sight: one in the upper right quadrant, one “in the right anterior axillary line 2cm below the costal margin, and one in the right midclavicular line.

6. **Exposure of calots**: The Gallbladder fundus is raised and retracted upward toward the right shoulder using an atraumatic grasper. It gives an adequate view of calot’s triangle and liver for dissection. Any adhesions if present between the liver and gallbladder are separated from the fundus towards the neck of the gallbladder using blunt dissection and cautery.

7. **Calot's Triangle Dissection**: After retraction of the infundibulum laterally for better visualization, the peritoneal layer over the neck of the gall bladder is exposed and opened.

8. **Obtaining a critical view of safety**: To prevent bile duct damage, it is important to thoroughly dissect the Calot's triangle and separate the infundibulum from the liver bed. Following dissection in Calot's triangle, only the cystic artery and cystic duct should be visible as they course toward the gallbladder. During ligation, two clips are applied to the side of the duct and one clip is applied to the side of the gallbladder over the cystic duct. Before placing clips, the stones located in the cystic duct, which connects to the gallbladder, are gently squeezed out. The cystic artery is ligated prior to the cystic" duct.

9. **Detachment of gallbladder from fossa**: Cystic plate is exposed after dissection of gall bladder fossa from its bed.

10. . **Extraction of gallbladder specimen**: The camera is placed in the subxiphoid port and the gallbladder after placing in endobag is removed from the umbilical port.

11. **Drainage and closure**: A drain is placed if bleeding from the liver bed is suspected and in case of iatrogenic bile spillage through gall bladder perforation.

D. BILE DUCT INJURY

The occurrence of bile duct injuries (BDI), which are uncommon but anticipated complications of cholecystectomy, has risen in tandem with the utilization of laparoscopic cholecystectomy for the management of symptomatic cholelithiasis. (5) The frequency of BDI was lower (0.1–0.2%) during the open cholecystectomy era, but it elevated around three times (0.4–0.6%) following the nearly widespread use of laparoscopic cholecystectomy, according to Kapoor et al. Since considerably greater rates are shown in prospective countrywide databases, these incidence rates are significantly underreported. These rates might be the result of an increase in both the quantity and complexity of surgeries.

Moghul and Kashyap, 2024 et al. have stated that the occurrence of BDI is computed to be between 0.3 & 0.7percent, which is approximately three times greater than in open cholecystectomy (19)

Iatrogenic bile duct injury, a significant contributor to illness and death, not only diminishes the patient's well-being but also escalates the likelihood of legal action against the surgeon if it remains undetected throughout the surgical procedure.

According to Lau et al. (2010), only 25–32.4% of biliary injuries were found after surgery. He went on to say that intraoperative discovery of BDI resulted in considerably better results and that the therapy of the injury was highly dependent on the timing of recognition as well as the type, extent, and severity of the injury. (20)

Anatomical variations, patient status, gallbladder pathology, and surgeon-related factors are risk factors for BDI. Variations in biliary anatomy and challenges in recognizing the biliary tree considerably increase the risk of intraoperative injury.(21)

Certain diseases increase the incidence of BDI and make biliary anatomy identification difficult. These include a short cystic duct, one that runs parallel to the common bile duct, changes at the cystic duct-CHD junction, insertion into the right hepatic duct, or accessory cystic ducts. (19)

Affected liver anatomical visualization can also be caused by obesity, previous hepatobiliary surgery, liver disease, either active or past, and acute cholecystitis in the past.

Moghul and Kashyap, (19)et all argued that bile duct injury was significantly higher about 3.5 times higher in patients with prior episodes of biliary inflammation as compared to patients with no prior inflammations. They postulated that episodes of inflammation lead to adhesions and altered anatomy leading to difficulty in visualization of biliary tree.(22)

Accordingly, it is generally agreed upon by numerous studies that a higher occurrence of BDI is associated with mistakes in the identification of biliary anatomy, which can result from a variety of contributing variables.

E. Intraoperative assessment of biliary anatomy

Thus in order to optimize the delineation of biliary anatomy, numerous methodologies have been deployed, encompassing

1. Intraoperative cholangiography (IOC)
2. Cholecystocholangiography (CCC)
3. Dye cholangiography
4. Near-infrared fluorescence cholangiography (NIRF-C)- ICG
5. Light cholangiography
6. Laparoscopic ultrasound (LUS)
7. Passive infrared cholangiography

1 **Intraoperative cholangiography (IOC)**

- The technique that is most frequently employed for intraoperative evaluation of the biliary anatomy is called IOC.

- The surgeon locates and inserts a cannula into the cystic duct where it connects to the gallbladder.
- After injecting radiopaque contrast into the cystic duct, X-ray fluoroscopy images are obtained.(23–25)

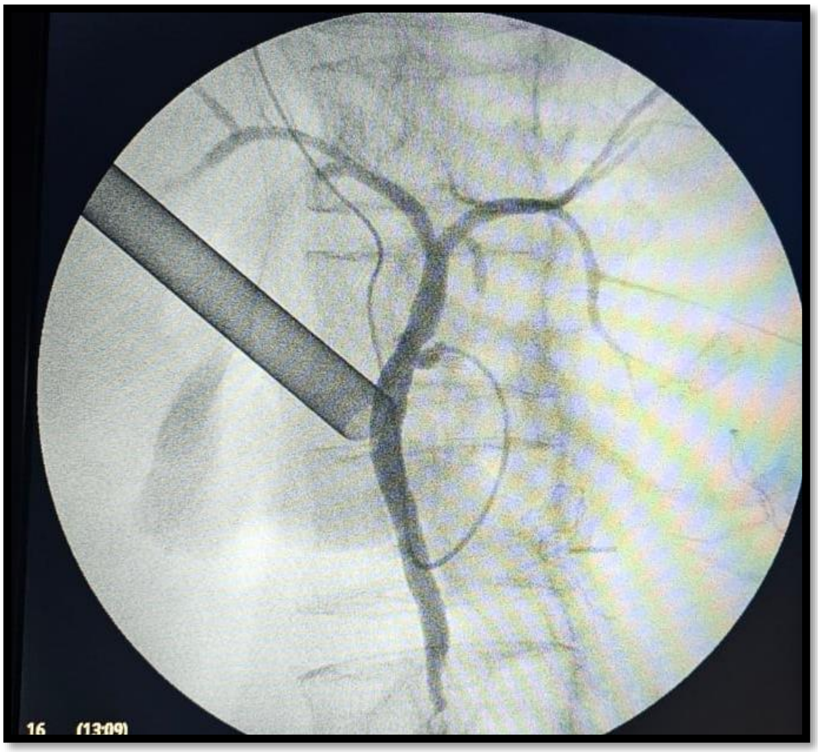


Image 7: Intraoperative cholangiography (IOC)

2 **Laparoscopic ultrasound (LUS)**

- A “laparoscopic flexible multifrequency ultrasonography transducer with Doppler flow detection technology and can visualize a tissue measuring 4 cm in length and 6 cm in depth.
- The transverse and longitudinal planes may be utilized to scan the extrahepatic bile ducts.
- LUS is able to recognize the hepatic artery, portal vein, inferior vena cava, ampulla, and the” bifurcation cystic duct-CBD.(26)

3 **Cholecystocholangiography (CCC)**

- The gallbladder is immediately injected with radiological contrast during the CCC procedure.
- In comparison to IOC, randomized controlled trials have revealed that CCC had a lower success rate.

4 **Dye cholangiography**

- According to reports, patients undergoing LC may benefit from intravenous injections of high dosages of methylene blue or indocyanine green (ICG) to identify their biliary structure.

5 **Light cholangiography**

- Through the papilla of Vater, an optic fiber is endoscopically inserted to light up the extrahepatic duct system.

6 **Passive infrared cholangiography**

- Warm saline is infused in the biliary tract and observed with a passive infrared camera to delineate the biliary anatomy
- However, this is a novel method still in the early phase of animal studies

7 **Near-infrared fluorescence cholangiography (NIRF-C)**

- In this method, fluorescent agents are excited by a laser, and the light that is subsequently released has a slightly higher wavelength, which is registered by an imaging filter.
- Human tissue has minimal absorbance and scattering of light and maximum penetration of light in the near-infrared (NIRF) spectrum (*800nm).

- Fluorophores that are eliminated via the liver, like IRDye 800CW "and Indocyanine green (ICG), can be administered either intravenously or directly into the biliary system for imaging" purposes.(27)

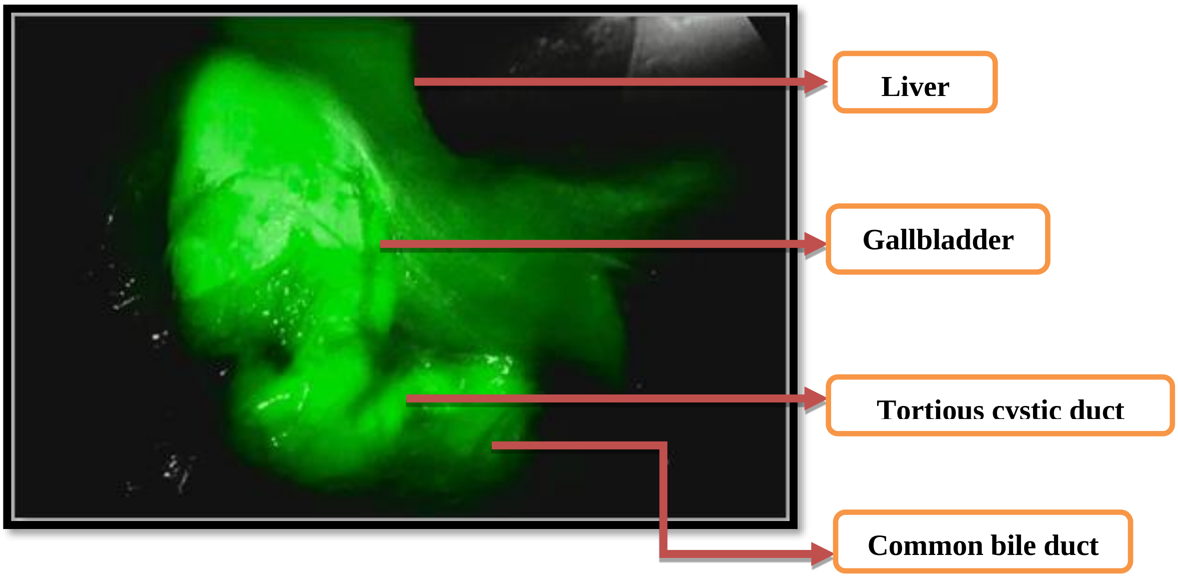


Image 8: Near-infrared fluorescence cholangiography (NIRF-C) with ICG

8 **Hyperspectral cholangiography**

- This technique depends on the various tissue absorption and reflection patterns.
- Requires absolutely no external contrast agent.
- However, this is a novel method still in the early phase of animal studies(23)

F. Near-infrared fluorescence cholangiography with Indocyanine green

An innovative technique for identifying and delineating biliary anatomy is NIRF-C with Indocyanine Green.

PHARMACOKINETICS.

- ICG is a water soluble tricarbocyanine dye
- Intravenous “injection of ICG dye, causes the blood to spread swiftly and uniformly after binding to albumin.
- Maximum absorption of the spectrum at 800 nm.
- The scientific name for Indocyanine Green is 1H-Benz[e]indolium.Two-[7[1,3-dihydro-1,1-dimethyl-3-(4-sulfobutyl)Indo-2-ylidene[-2Hbenz[e]]Phenatrienyl-1,3,5sodium, inner salt, -1,1-dimethyl-3-(4-sulfobutyl)-,hydroxide. Indolin-2-ylidene 2-[7-[1,1-Dimethyl-3-(4-sulfobuttyl)benz[e]Phenatrienyl-1,3,51-(4-sulfobutyl)-1,1-dimethyl-3-sodium” salt, inner salt, -1Hbenz[e]indolium hydroxide.
- Ph of 6.5 after reconstitution
- After an intravenous infusion, albumin is the main carrier of ICG, which is quickly bound to plasma protein (95%).
- It does not undergo any extrahepatic or enterohepatic circulation;
- It has very little dye uptake in the kidneys, lungs, peripheral blood, or brain.
- The ICG is only taken up by the parenchymal cells of the liver and is fully secreted into the bile. and then eliminated by the bile.

Despite a considerable difference in the computed value for clearance, women have a higher plasma fractional disappearance rate than men.

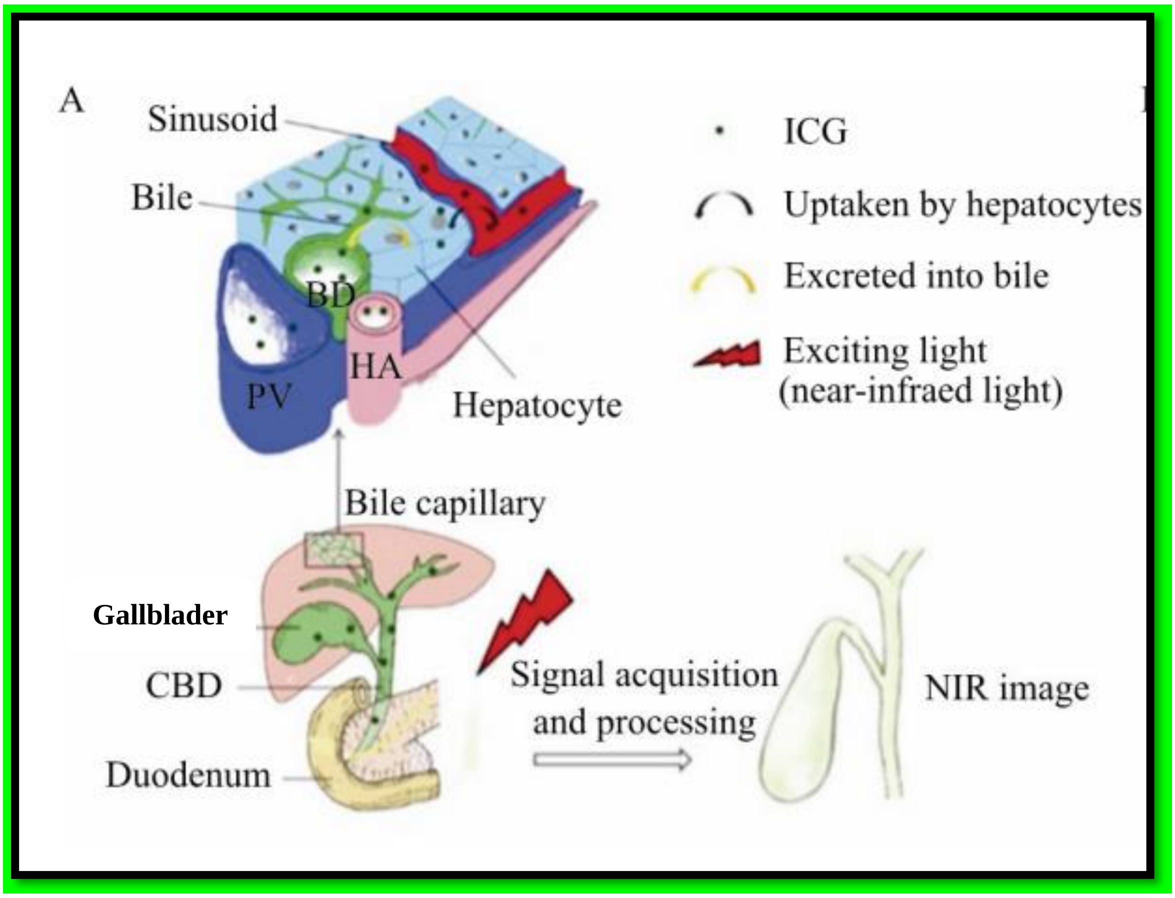


Image 9: Pharmacokinetics of ICG

After attaching to plasma proteins, Indocyanine green (ICG) fluoresces brightly, peaking at about 830nm when exposed to near-infrared (NIR) light.

This property of ICG of fluorescence in the near-infrared spectrum can be utilized and with the help of special NIRF cameras, the fluorescence can be picked up

Ishizawa et al. initially described fluorescence intraoperative cholangiography (IOC) techniques employing intrabiliary or intravenous administration of ICG to visualize the architecture of extrahepatic bile ducts during both open and laparoscopic cholecystectomy. Their findings suggested that this approach holds promise for hepatobiliary surgical procedures. (28)

Ambe et al.'s 2019 study analyzed patient data “to compare the outcomes of laparoscopic cholecystectomy with and without the use of indocyanine green (ICG). The investigation found that combining laparoscopic cholecystectomy with real-time indocyanine green fluorescence cholangiography improves the visualization and identification of the biliary tree. Therefore, this technique should be considered” to enhance the safety of laparoscopic cholecystectomy (29)

ICG was utilized during every laparoscopic cholecystectomy in this investigation. An intravenous infusion of 0.5ml of ICG was administered one hour before surgery.

The optimal timing for preoperative administration of the dye remains undefined, with studies ranging from on-table intravenous injection of ICG to preoperative use of ICG 24 hours prior to surgery.

Ambe et al., 2019 used 1 hour to 1.5 hrs pre-operative use of ICG, and Obonna 2020 et al. used 45 mins preoperative use of ICG(9,29). Both these studies had similar findings

A systematic review by Boogerd et al. (2017) found twenty- trials with 1057 patients. The bulk of research employed 2.5mg given one hour before imaging. The clinical research findings indicated that the highest ratio of fluorescence between the bile duct and liver was achieved within a time frame of 3-7 hours after administering 5 mg of ICG, and within a time frame of 5-25 hours after administering 10mg of ICG. Up to three hours after administering 5 mg of ICG, the liver exhibited fluorescence that was equal to or greater than the fluorescence of the cystic duct. Similarly, up to five hours after administering 10 mg of ICG, the liver continued to exhibit fluorescence (30)

Determining the efficacy of NIRF-C employing Indocyanine Green in laparoscopic cholecystectomies is the goal of this study.

MATERIAL METHODS

Source of Data: Data was collected from patients KLE's Dr. Prabhakar Kore Hospital and medical research centre.

Study Design: Observational study

Study Period: 1 YEAR

Sample Size: The formula used for sample size calculation is,

$$n = \left(\frac{Z_{\alpha/2} * \sigma}{d}\right)^2$$

where σ is the expected standard deviation of the population, d is the acceptable margin of error, and for a 95% confidence level, $Z\alpha/_2$ value is 1.96.

The length of stay was observed to be in the range of 2 to 17 days for the subjects undergoing laparoscopic cholecystectomy. Based on the range rule of thumb, the standard deviation will be 3.75. With a precision of 25% of the standard deviation and a similar outcome at the 95% confidence level, the sample size is determined by,

$$n = \left(\frac{1.96 * 3.75}{0.9375}\right)^2$$

$$n = 61.4656 \approx 62$$

Thus, sixty-two individuals are the minimal sample size needed. The precision increases with the sample size.

Sampling technique: Simple random sampling

Inclusion Criteria:

1. Patient undergoing laparoscopic cholecystectomy for symptomatic cholelithiasis and cholecystitis
2. Patient age more than or equal to 18 years of age
3. ASA classification of physical status 1 or 2 with normal kidney and liver functions\

Exclusion Criteria:

1. Patient with liver cirrhosis .
2. Patients “with a history of Hepatitis B and C and bleeding disorders
3. Patient with a history of allergy to the dye
4. Patient undergoing laparoscopic cholecystectomy for diseases other than symptomatic cholelithiasis and cholecystitis

Study protocol: The Dr. Prabhakar Kore Hospital and Medical Research Center in Belagavi, Karnataka, is home” to KLE's inpatient surgery department, where the cross-sectional investigation was carried out. Participants will get information about the investigation. Subjects who voluntarily agreed to participate were given written informed consent. In line with the subject's preferred or known language, informed consent was given.

a) Preoperative Indocyanine dye was administered to 50% of the randomly selected patients undergoing laparoscopic cholecystectomy.

b) The procedure of injecting dye – The Indocyanine dye was injected 1 hour 30 minutes -2 hours preoperatively. Indocyanine dye under the brand name AUROGREEN was utilized

c) The AUROGREEN powder was reconstituted with 10ml sterile water and diluted to a level 1: 10 concentration

d) A test dose of 0.1 cc was injected IV and the patient was observed for any allergic reactions

e) A full dose of 1ml ie. 2.5mg was injected IV about 1 hour 30 minutes to 2 hours prior to the surgery

Image 10: Intravenous injection of ICG via Micro-filter.

f) A standard 4-port American technique for laparoscopic cholecystectomy was used.(31)

g) The entire procedure was recorded for further data collection and analysis

h) The hepatic, cystic, and common bile ducts were among the anatomical features of the biliary tree that were periodically observed using an infrared camera.

i) Stryker 1588 AIM laparoscopic system was used for the procedure.

j) The time taken to identify the critical view of safety (CVS) once the gall bladder was retracted over the liver was measured.

k) After surgery, the patient was monitored for a total of 14 days to evaluate any problems.

Data collection procedure:

a. Demographic data age, height, weight, and gender were collected

b. Using the procedure's recorded video, data on “the visualization of the biliary structures and the amount of time needed to achieve the critical view of safety were gathered.

The data collected was tabulated and charted

DATA ANALYSIS PLAN:

Microsoft Excel and the statistical program R version 4.2.1 was utilized to examine the data. Categorical variables will be represented using frequency tables. For continuous values, the “Mean ± SD / Median (Min, Max) form will be used. To determine whether qualities are related, the Chi-Square test will be utilized. The QQ plot and the Shapiro-Wilk test are used to determine whether a variable is normal. The means of the variables across groups are compared using the 2-sample t-test. Mann-Whitney U test To assess the distribution of variables among different groups, employ the U test. A $P \leq 0.05$ indicates statistical significance.

RESULTS

The” study covered 68 patients in total. Of the total 68 patients, 50% that is 34 of the patients received Indocyanine green dye preoperatively.

Study population (N=68) group descriptive analysis

Table 1- Study population.

Study Group		**Frequency**	**Percentages**
Group A	Intervention- with ICG dye	34	50.00%
Group B	Control- without ICG dye	34	50.00%

Group A was patients with ICG dye and

Group B was patients without ICG dye.

The patients in the ICG group received the dye 1.5-2 hours preoperatively after a test dose.

Of the two groups, demographic parameters like age, sex, weight, and BMI were comparable.

Data contains measurements on 68 subjects, with an equal distribution of 34 (50%) subjects in group A & 34 (50%) subjects in group B.

The investigation group consisted of 36 female participants and 32 male individuals. The individuals were randomly divided into two groups.

All the participants in this study were adults with an age span ranging from 22 to 78 years of age

The following table gives the comparison of demographic variables over groups.

Table 2: Comparison of demographic variables over "groups.

Variables	Sub Category	Group A	Group B	Total	p-value
Age (years)	Mean ± SD	45.29 ± 15.62	50.91 ± 10.85	48.1 ± 13.64	0.0903^{Wt}
	Median (Min, Max")	45 (22, 78)	52 (27, 73)	47.5 (22, 78)	
Sex	Female	22 (64.71%)	14 (41.18%)	36 (52.94%)	0.0519^{C}
	Male	12 (35.29%)	20 (58.82%)	32 (47.06%)	
Weight (Kg)	Mean ± SD	68.94 ± 8.11	70.41 ± 12.41	69.68 ± 10.43	0.5651^{Wt}
	Median (Min, Max)	69.5 (48, 82)	69.5 (45, 97)	69.5 (45, 97)	
Height (cm)	Mean ± SD	162.09 ± 7.34	167.88 ± 6.76	164.99 ± 7.59	0.0012^{t*}
	Median (Min, Max)	160 (146, 178)	168 (154, 180)	166 (146, 180)	

*Abbreviation: C – Chi-square test, Wt – Welch's t-test, t – Two sample t-test, * indicates statistical significance.*

Group B's mean age is 50.91 ± 10.85 years, while Group A's mean age is 45.29 ± 15.62 years. Group A's and Group B's median ages are 45 and 52 years old, respectively. Welch's t-test results show that the age distributions of the groups do not differ significantly (p-value = 0.0903).

In terms of sex distribution, Group A has a higher proportion of females (64.71%) compared to Group B (41.18%), while Group B has more males (58.82%) than Group A (35.29%). Based on the Chi-square test outcomes, there is no significant variation in the sex distributions of the groups (p-value = 0.0519).

With a median weight of 69.5 kg, Group A's mean weight is 68.94 ± 8.11 kg, while Group B's mean weight is 70.41 ± 12.41 kg. There isn't a significant difference between the groups, according to Welch's t-test results (p-value = 0.5651).

For height, Group A's mean height is 162.09 ± 7.34 cm and Group B's mean height is 167.88 ± 6.76 cm, with medians of 160 cm and 168 cm, respectively. The results of the two sample t-tests show that the groups' differences in height are statistically significant (p-value = 0.0012).

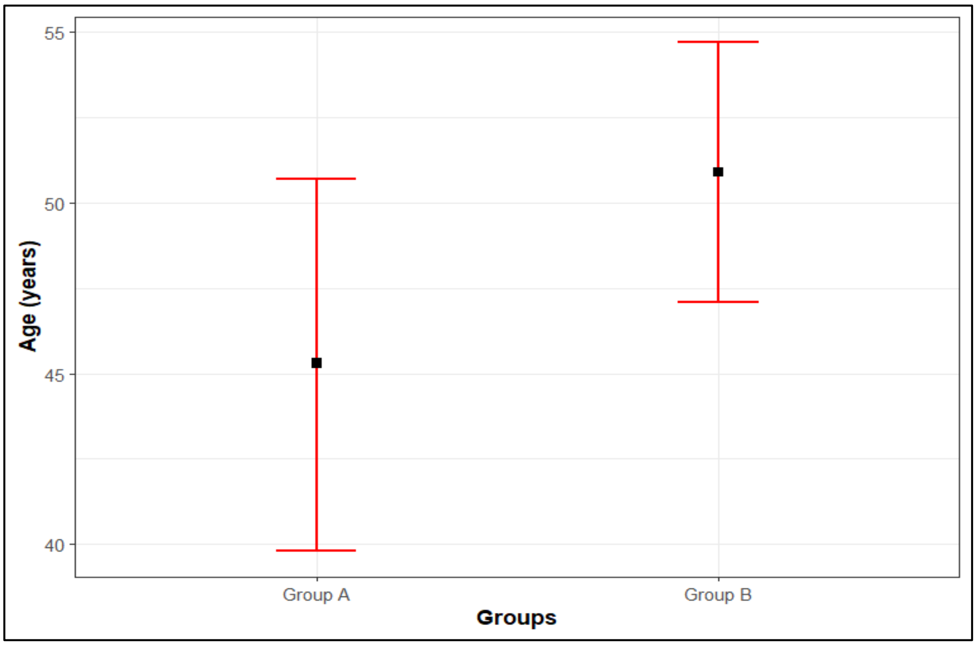


Figure 1: Mean plot of age over groups.

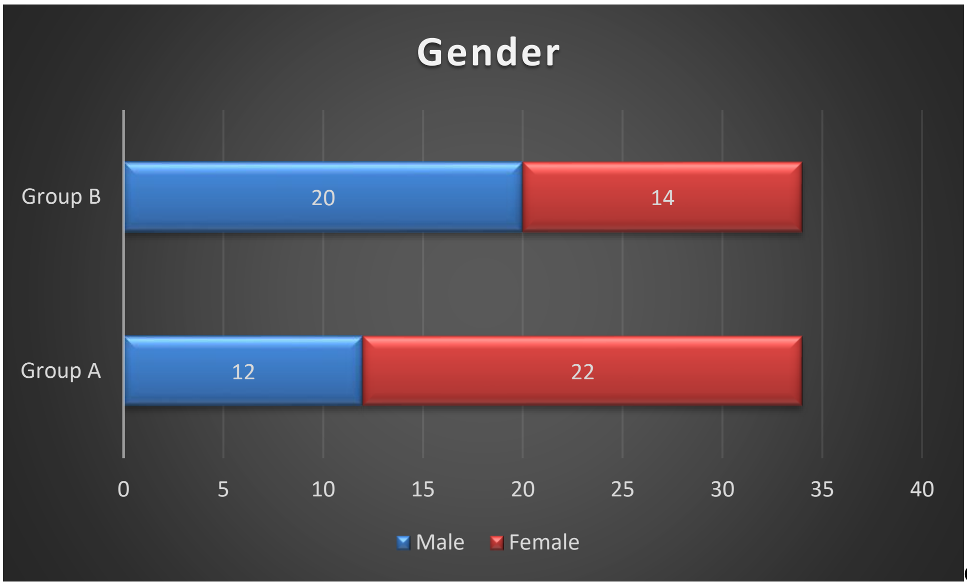


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Figure 2: Distribution of gender in both groups.

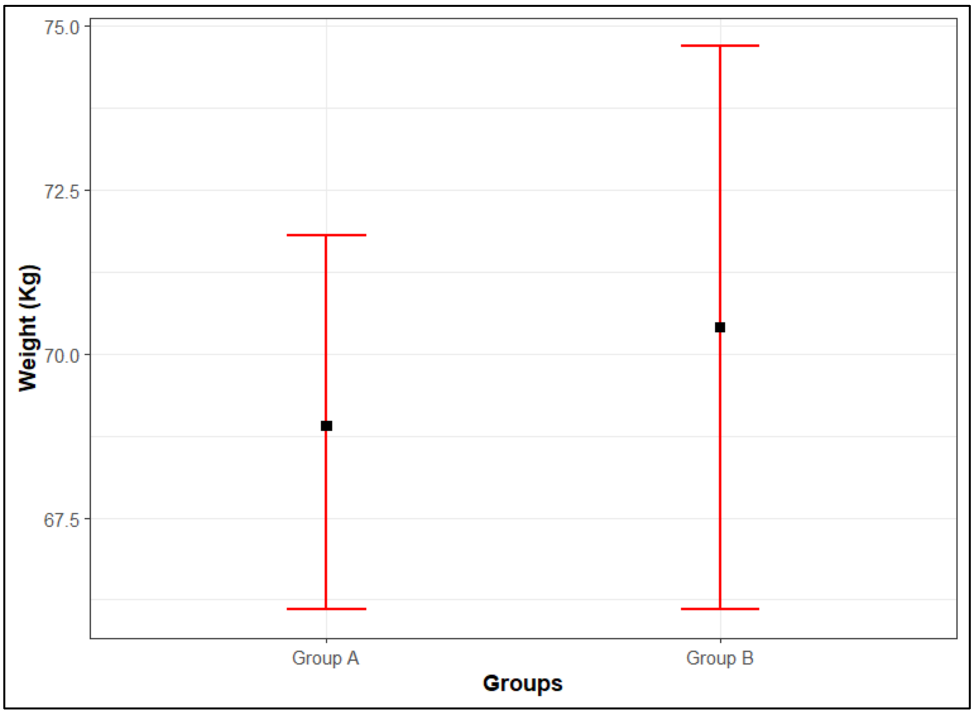


Figure 3: Mean plot of weight over groups.

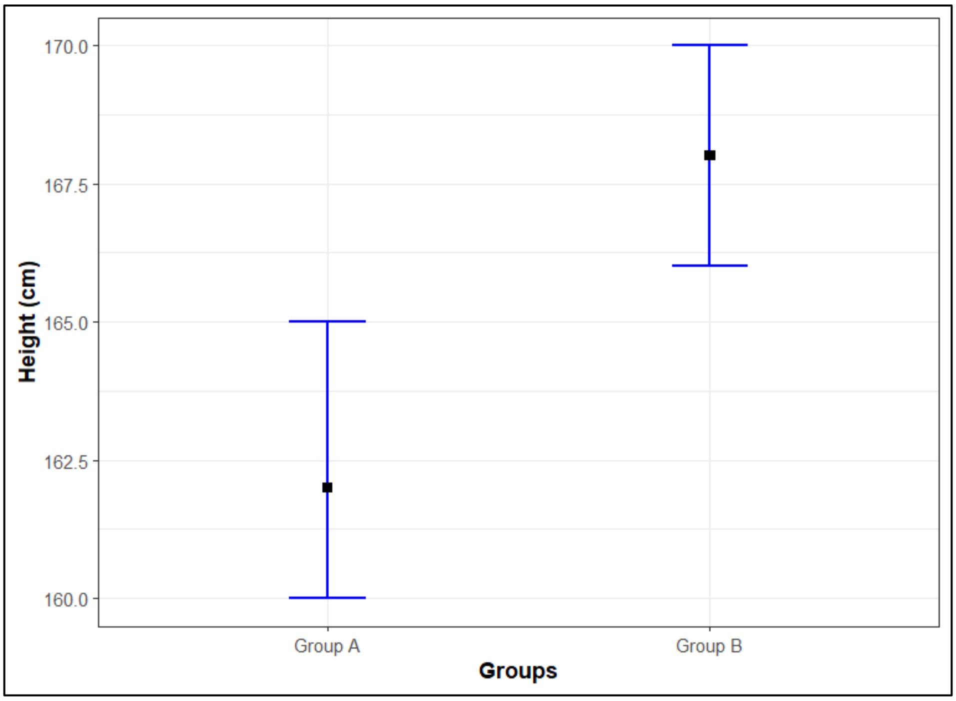


Figure 4: Mean plot of height over groups.

The following table gives a comparison of medical history over groups.

Table 3: Comparison of medical history "over groups.

Variables	Sub Category	Group A	Group B	Total	p-value"
Previous history of acute cholecystitis	No	17 (50%)	19 (55.88%)	36 (52.94%)	0.6270[C]
	Yes	17 (50%)	15 (44.12%)	32 (47.06%)	
Choledocholithiasis	No	31 (91.18%)	31(91.18%)	62 (91.18%)	0.2454[MC]
	Yes	3 (8.82%)	3(8.82%)	6 (8.82%)	

Abbreviation: C – Chi-square test, MC – Chi-square test with Monte Carlo simulation.

The patients included in this study were symptomatic for cholelithiasis with 47% of the patients having previous single or multiple attacks of acute cholecystitis.

For acute cholecystitis, both groups have similar distributions, with 50% of Group A and 55.88% of Group B having no prior history of the condition. Group B has a proportion of 44.12% while Group A has a proportion of 50% among individuals with a history of acute cholecystitis. The Chi square test outcomes indicate that there is no statistically significant disparity in the previous occurrences of acute cholecystitis among the groups (p-value = 0.6270).

The patients were operated at an approximate interval of 6 weeks after the previous attack of acute cholecystitis.

Out of the 32 patients who had a history of acute cholecystitis, only two underwent surgery during the first 72 hours of the acute phase.

Interestingly both these patients were in the ICG group and did not show any uptake of Indocyanine green dye.

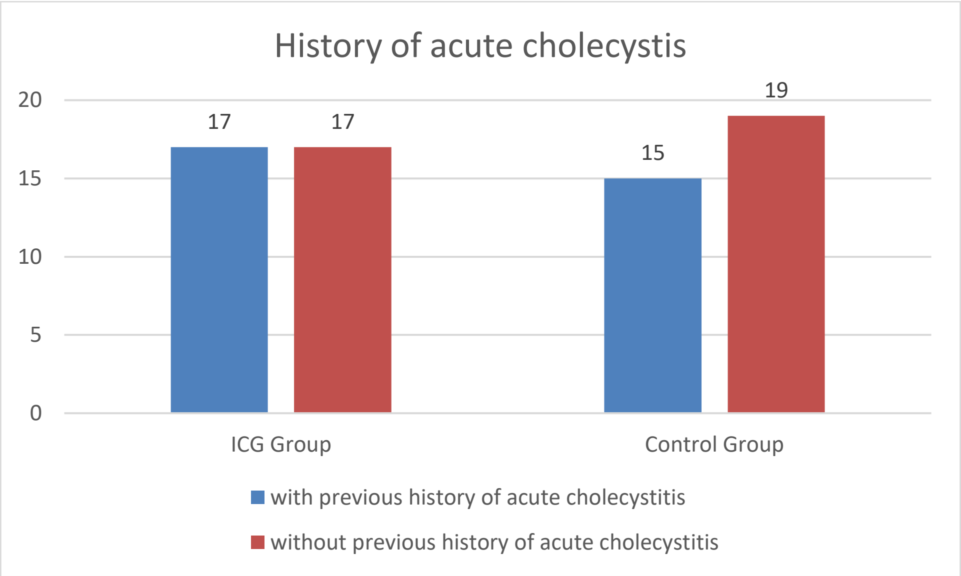


Figure 5: Distribution of acute cholecystitis in both groups.

All the patients underwent a preoperative ultrasonography with a majority that is 62 of the 68 patients suffering from cholelithiasis with 91.18% of the "patients in Group A and Group B had only cholelithiasis, while 8.82% of Group A and Group B having choledocolithiasis. The Chi-square test outcomes indicate that there is no statistically significant difference between the groups for this condition (p-value = 0.2454").

All 6 patients with choledocolithiasis underwent ERCP with stent placement preoperatively. And were subsequently taken up for laparoscopic cholecystectomy.

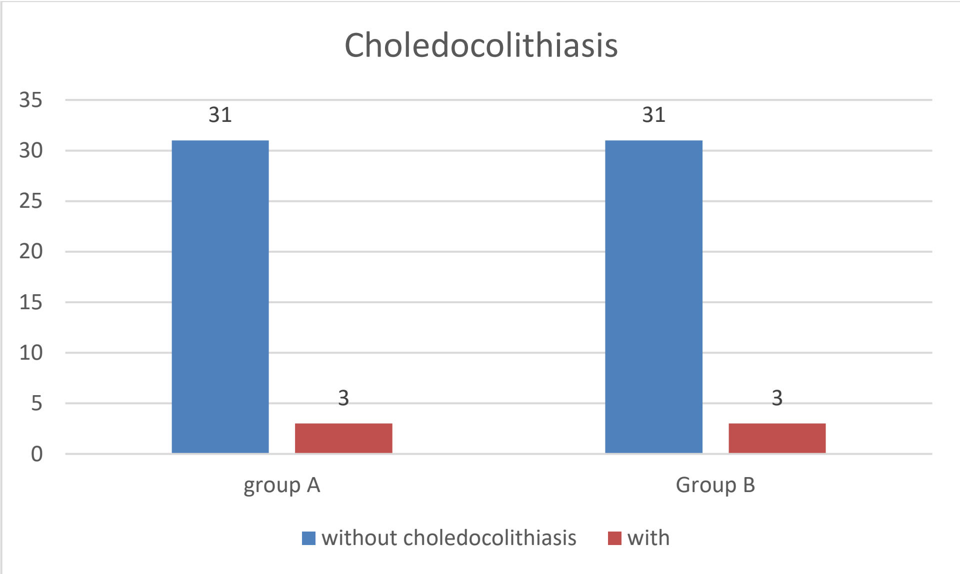


Figure 6: Distribution of choledocolithiasis in both groups.

The following table gives the “comparison of intraoperative findings between the 2 groups.

Table 4: Comparison of intraoperative findings over groups.

Variables	Sub Category	Group A	Group B	Total	p-value
Identification” of cystic duct	No	6 (17.65%)	7 (20.59%)	13 (19.12%)	0.7578^{C}
	Yes	28 (82.35%)	27 (79.41%)	55 (80.88%)	
Identification of CBD	No	11 (32.35%)	19 (55.58%)	28 (44.11%)	0.050^{C}
	Yes	23 (67.65%)	15 (44.11%)	40 (55.88%)	
Identification of hepatic duct	No	15 (44.12%)	22 (64.71%)	37 (54.41%)	0.0883^{C}
	Yes	19 (55.88%)	12 (35.29%)	31 (45.59%)	
Identification of cystic artery	No	3 (8.82%)	5 (14.7%)	8 (11.76%)	0.452^{C}
	Yes	31 (91.18%)	29 (85.29%)	56 (88.23%)	
Total time of surgery	Mean ± SD	58.44 ± 17.44	77.38 ± 22.63	67.91 ± 22.2	0.0003^{t*}
	Median (Min, Max)	59 (18, 88)	77 (38, 124)	67.5 (18, 124)	
Identification of Critical Angle	Could not be identified	4 (11.76%)	7 (20.59%)	11 (16.18%)	0.3232^{C}
	Identified	30 (88.24%)	27 (79.41%)	57 (83.82%)	
Time to identify critical angle of safety	Mean ± SD	24.2 ± 11.93	36.78 ± 18.95	30.16 ± 16.75	0.0062^{MW} *
	Median (Min, Max)	23 (2, 54)	32 (12, 87)	25 (2, 87)	
Conversion to open	No	33 (97.06%)	33 (97.06%)	66 (97.06%)	0.9999^{MC}
	Yes	1 (2.94%)	1 (2.94%)	2 (2.94%)	

*Abbreviation: "C – Chi-square test, MC – Chi-square test with Monte Carlo simulation, t- Two-sample t-test, MW – Mann Whitney U test, * indicates statistical significance.*

Regarding the identification of anatomical structures such as the cystic duct, cystic artery, and hepatic duct, the Chi-square test results show no significant differences between the groups (p-values > 0.05"), however the identification of CBD was considerable better in Group A with a p value of 0.05 with was statically significant.

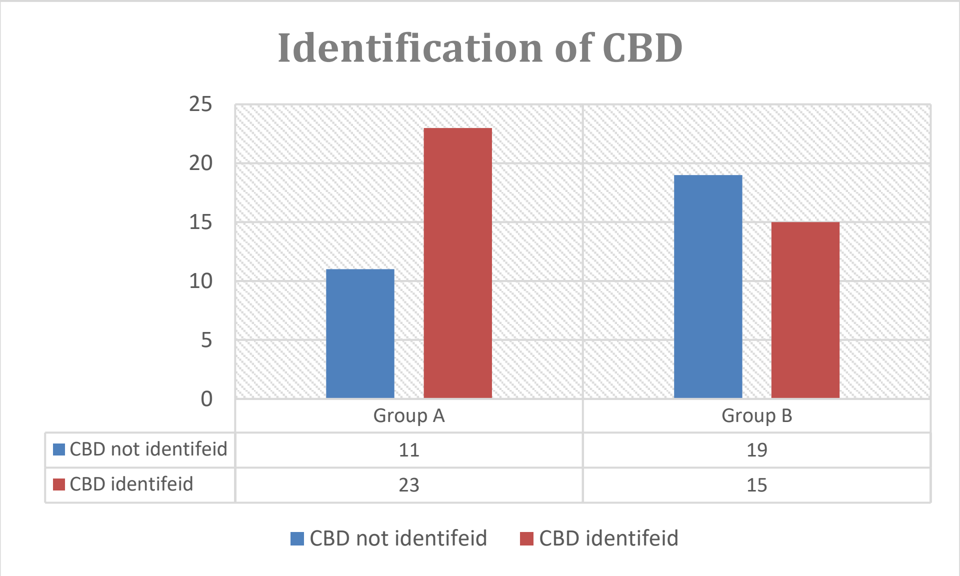


Figure 7: Distribution of identification of CBD in both groups

From the two sample t-tests, it is observed that the total time of surgery is significantly different between the groups (p-value = 0.0003), with Group B having a longer mean time compared to Group A. Furthermore, the Mann-Whitney U test demonstrates a significant difference (p-value = 0.0062) in the amount of time needed to identify key angles, with Group B requiring longer than Group A on average.

There was no discernible difference between the two groups' conversion rates to open surgery (p-value = 0.9999).

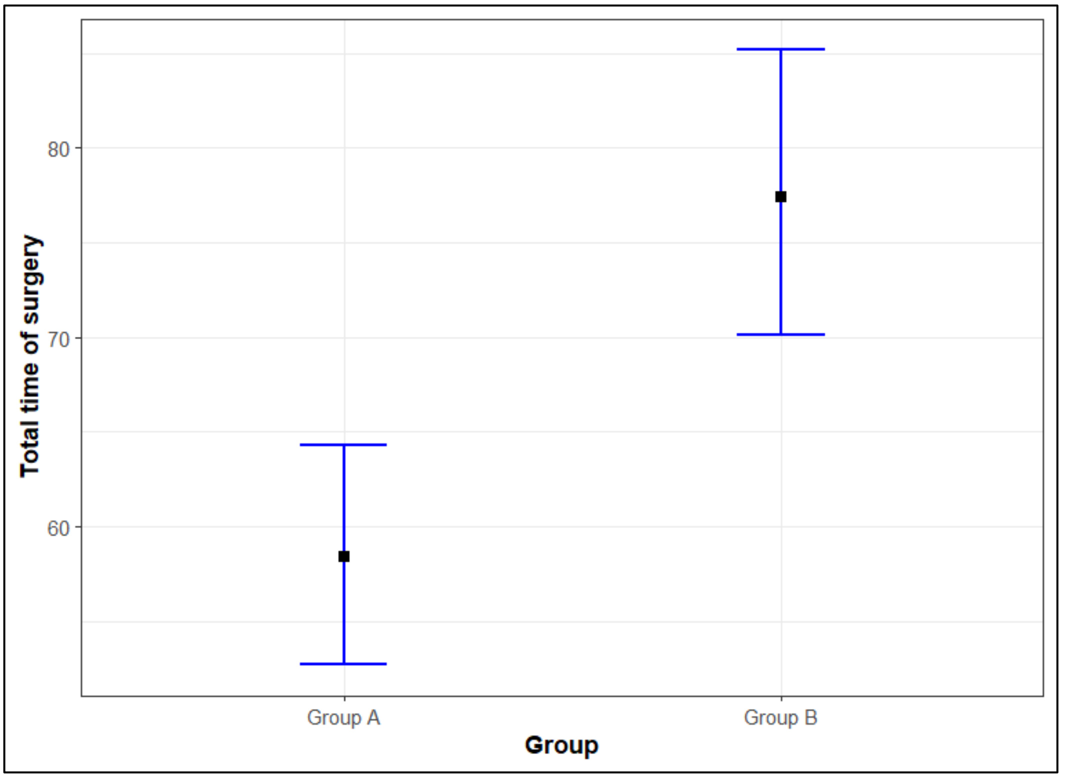


Figure 8: Mean plot of total time of surgery over groups.

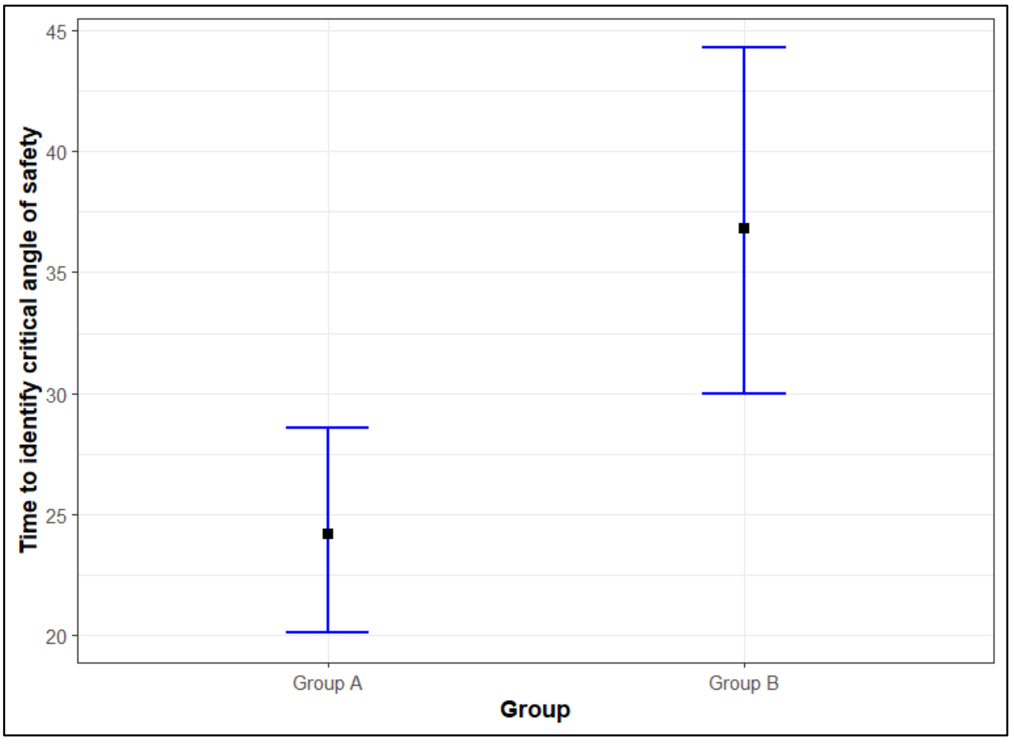


Figure 9: Mean plot of time to identify critical angle of safety over groups.

Table 6: Comparison of Surgery details and post-operative details “over groups.

Variables	Sub Category	Group A	Group B	Total	p-value
Post-operative bile leak	No	34 (100%)	33 (97.06%)	67 (98.52%)	0.5052MC
	Yes	0	1 (2.94%)	1 (1.47%)	
The mean duration of stay(days)	Mean ± SD	4.47 ± 1.91”	4.88 ± 2.07	4.68 ± 1.99	0.3763MW
	Median (Min, Max)	4 (3, 11)	4 (3, 11)	4 (3, 11)	
Type of surgery performed	Cholecystectomy	30 (88.24%)	27 (79.41%)	57 (83.82%)	0.7356MC
	Lap subtotal cholecystectomy	3 (8.82%)	6 (17.65%)	9 (13.24%)	
	Open subtotal cholecystectomy	1 (2.94%)	1 (2.94%)	2 (2.94%)	
Allergic Reaction	NIL	34 (100%)	34 (100%)	68 (100%)	1C

Abbreviation: “C – Chi-square test, MC – Chi-square test with Monte Carlo simulation, MW – Mann Whitney U test.

Based on the Chi-square test, 100% of patients in Group A and 94.12% in Group B did not have a postoperative bile leak (p-value = 0.5052). This indicates that there is no significant difference in the incidence of postoperative bile leaks between the two groups.

The mean length of hospital stay did not substantially differ between Group A and Group B, according to the Mann-Whitney U test. Both groups had similar mean durations of stay (4.47 ± 1.91 days for Group A and 4.88 ± 2.07 days for Group B) (p-value = 0.3763).

With 88.24% of patients in Group A and 79.41% in Group B undergoing cholecystectomy, the majority of patients in" both groups underwent this type of surgery. Furthermore, a small number of patients received open or lap partial cholecystectomy in each group. The distribution of the type of operation conducted among groups does not differ significantly, according to the results of the Chi-square test (p-value = 0.7356).

Lastly, both Group A & Group B had no reports of allergic reactions post-surgery, with 100% of patients in both groups having no allergic reactions (p-value = 1).

The following table gives the comparison of laboratory parameters over groups.

Table 7: Comparison of laboratory parameters over "groups.

Variables	Group A	Group B	Total	p-value
Haemoglobin"	12.49 ± 1.56 12.3 (8.3, 15.7)	12.17 ± 2.09 12.45 (6.9, 16.4)	12.33 ± 1.84 12.35 (6.9, 16.4)	0.4838^{t}
TLC	8.63 ± 3 7.6 (5.29, 17.5)	8.86 ± 3.09 8.3 (3.8, 21.2)	8.75 ± 3.02 7.95 (3.8, 21.2)	0.4430^{MW}
Platelet	272.53 ± 93.74 255 (105, 565)	270.12 ± 85.16 262 (95, 565)	271.32 ± 88.89 258 (95, 565)	0.8444^{MW}
Total Bilirubin	0.78 ± 0.61 0.64 (0.18, 2.74)	0.86 ± 0.61 0.62 (0.18, 2.62)	0.82 ± 0.61 0.63 (0.18, 2.74)	0.6811^{MW}
Direct Bilirubin	0.37 ± 0.38 0.25 (0.03, 1.94)	0.49 ± 0.41 0.26 (0.04, 1.62)	0.43 ± 0.4 0.25 (0.03, 1.94)	0.2174^{MW}
Indirect Bilirubin	0.43 ± 0.29 0.36 (0.09, 1.3)	0.4 ± 0.29 0.32 (0.06, 1.48)	0.41 ± 0.29 0.34 (0.06, 1.48)	0.5234^{MW}

SGOT	29.03 ± 18.95 21.5 (14, 108)	33.35 ± 44.07 23 (9, 269)	31.19 ± 33.73 22.5 (9, 269)	0.5847^{MW}
SGPT	27.97 ± 20.31 22 (10, 112)	32.35 ± 31.79 23.5 (14, 190)	30.16 ± 26.57 23 (10, 190)	0.3054^{MW}
ALP	99.03 ± 36.1 91.5 (34, 208)	122.03 ± 125.35 91 (39, 787)	110.53 ± 92.28 91 (34, 787)	0.3076^{MW}
Total Protein	7.13 ± 0.58 7.1 (5.1, 8.1)	6.73 ± 1.32 7 (0.5, 8.1)	6.93 ± 1.03 7.05 (0.5, 8.1)	0.1451^{MW}
Serum Albumin	4.17 ± 0.5 4.2 (2.65, 4.8)	4 ± 0.53 4 (2.4, 4.8)	4.08 ± 0.52 4.2 (2.4, 4.8)	0.1241^{MW}

*Abbreviation: "t- Two-sample t-test, MW – Mann Whitney U test, * indicates statistical significance.*

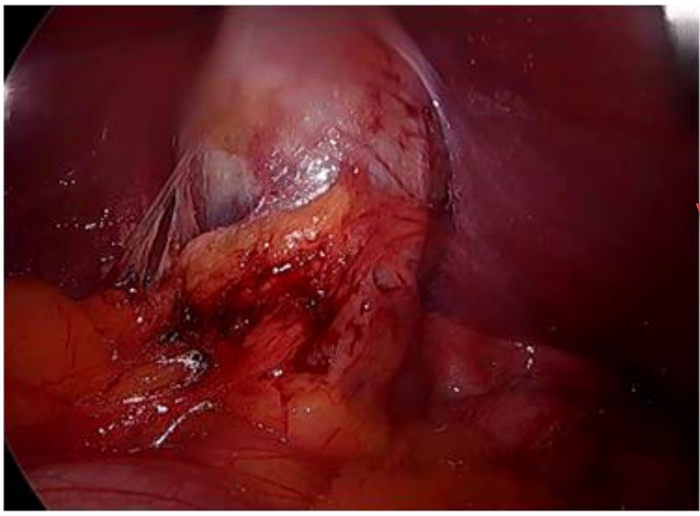
The two groups did not differ statistically in terms of hemoglobin levels, total leukocyte count (TLC), platelet count, total bilirubin, direct bilirubin, indirect bilirubin, SGOT, SGPT, ALP, total protein, and serum" albumin.

DISCUSSION

One of the most popular surgical treatments is laparoscopic cholecystectomies, with safe cholecystectomy practices being widely used. Avoiding biliary injury during an elective cholecystectomy is of utmost importance.

The use of ICG dye with NIRF imaging provides a significant guiding tool in the armament of the surgeon while performing a laparoscopic cholecystectomy.

In this study, ICG helped in successfully identifying the extrahepatic biliary structures with an identification rate for cystic duct at 82.35% and for CBD being 67.65%. Although the identification rate for cystic duct was comparable to the control group, but the identification of CBD was significantly better in the ICG group with a P value of 0.05 which was statically significant. Although the cystic duct identification rates were comparable, the ease of identification was much better with the use of ICG.



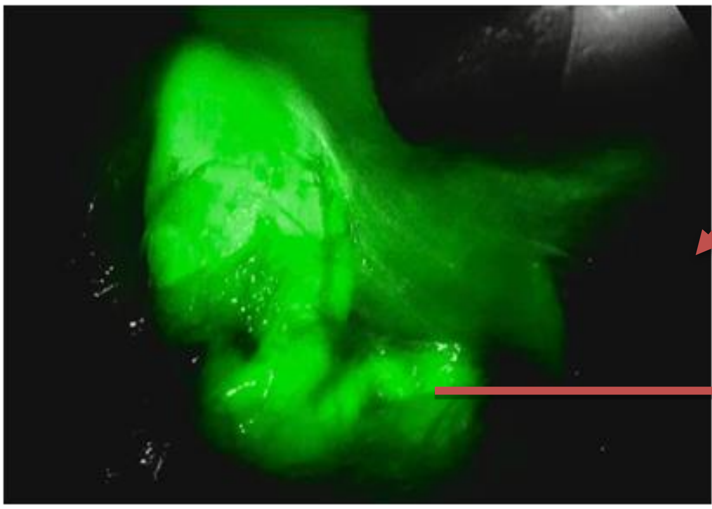


Image 11: comparison between visualization of biliary anatomy with and with and without use of ICG.

Tortious cystic dust and CBD better seen with ICG

Successful dissection of the calots triangle without injuring the CBD and hepatic duct is the most crucial step in any cholecystectomy. This is a challenging endeavor faced by surgeons especially in difficult gallbladders. Thus with a higher identification rates for CBD, the dreaded complication of BDI during laparoscopic cholecystectomy can be averted with ICG by providing better guidance while dissecting the calots triangle.

CBD and cystic duct visualized significantly better

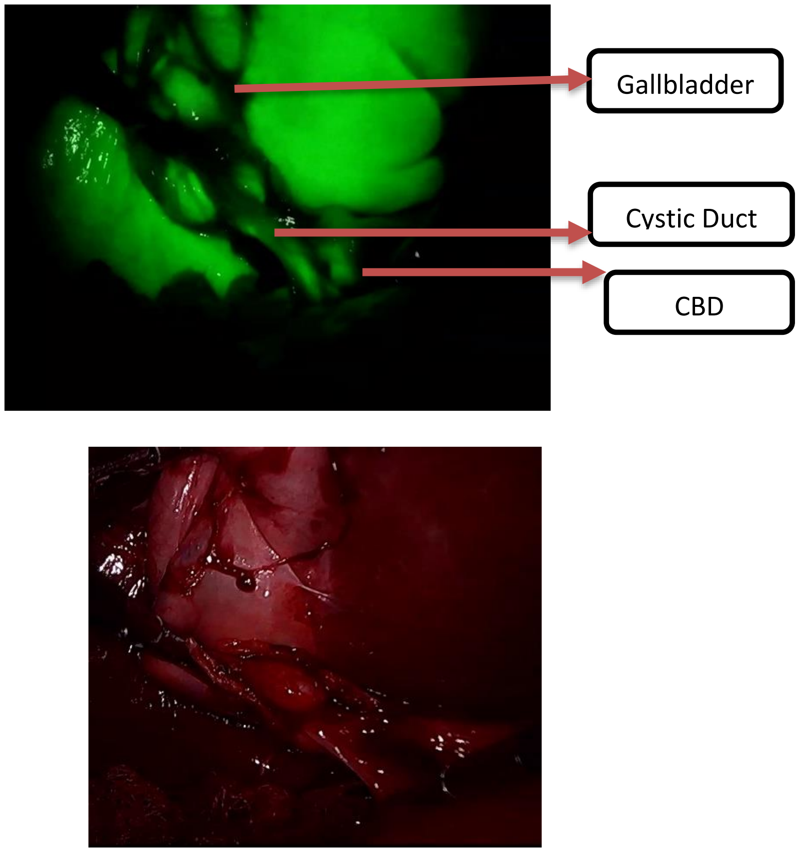


Image 12: Better visualization of cystic duct and CBD with the use of ICG.

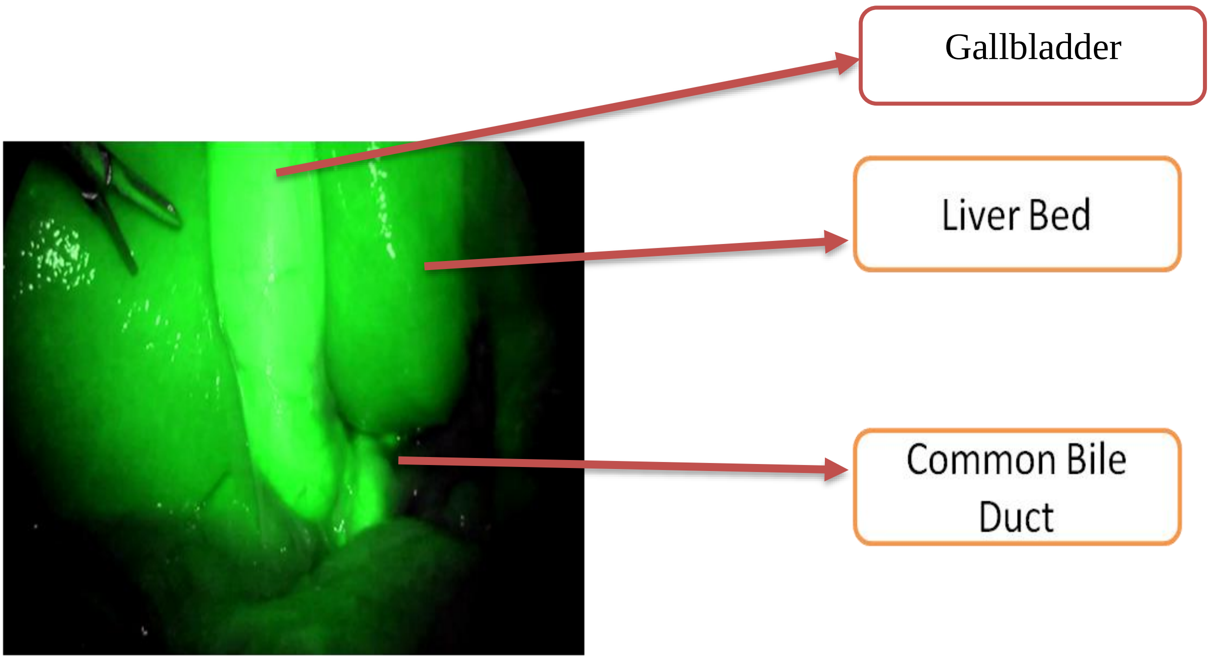


Image 13: Visualization of CBD with the use of ICG.

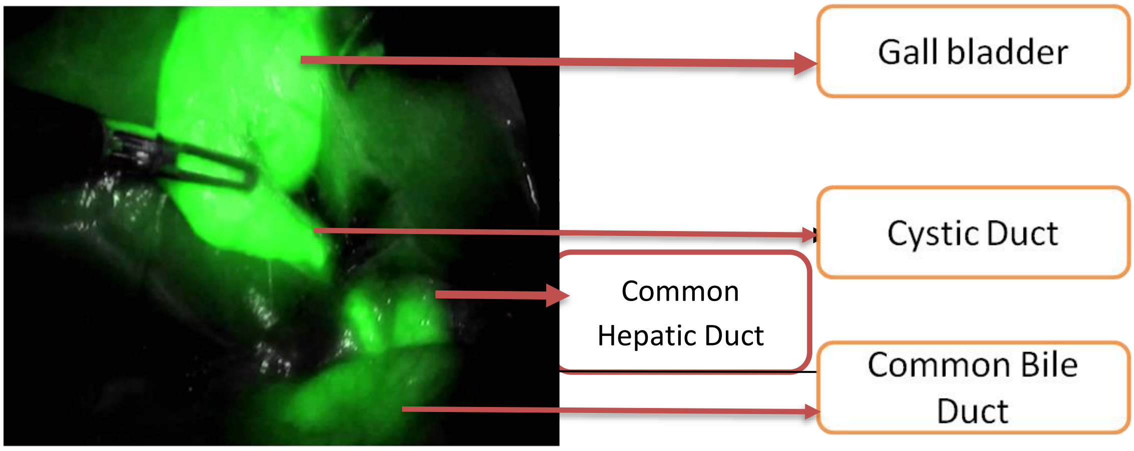


Image 14: Visualization of CBD and CHD with the use of ICG.

Comparable research by Ambe et al. and Obonna and Obonna, 2020 only identified the cystic duct and suggested that a successful identification would improve surgical results; however, the precise rates of structural identification were not stated.

A prospective analysis done by Obonna and Obonna, 2020 only showed successful identification of biliary structures which was consistent with our results. (9,18), however, none of these studies exactly mention the rates of identification of biliary structures.

A systemic review of studies using ICG for LC conducted by Vlek et al., 2017 (32) showed that the mean identification rates for cystic ducts ranged between 71.2–96.6 which was comparable to our study. However, the meta-analysis showed a higher rate of identification of CBD with mean rates ranging between 67.1–98.0% which were also comparable to our study. However, these studies did not take into account the factors influencing the identification of biliary structures.

Symeonidis et al,Conducetd a study to compare the effectiveness between IOC and NIRF-C and found that both had similar results(33)

Interestingly it was observed that of the two cases that were operated in the early acute phase of cholecystitis, no illumination of extrahepatic biliary tree or gall bladder was observed. However adequate illumination of the liver was noted, Which leads to suggests that poor fluorescence and poor identification may be seen in edematous and inflamed biliary tissues. A higher dosage of ICG might be required in such cases as suggested by Vlek et al.(32)

These findings were further confirmed by the correlation between elevated total leucocyte counts in cases where fluorescence was not observed.

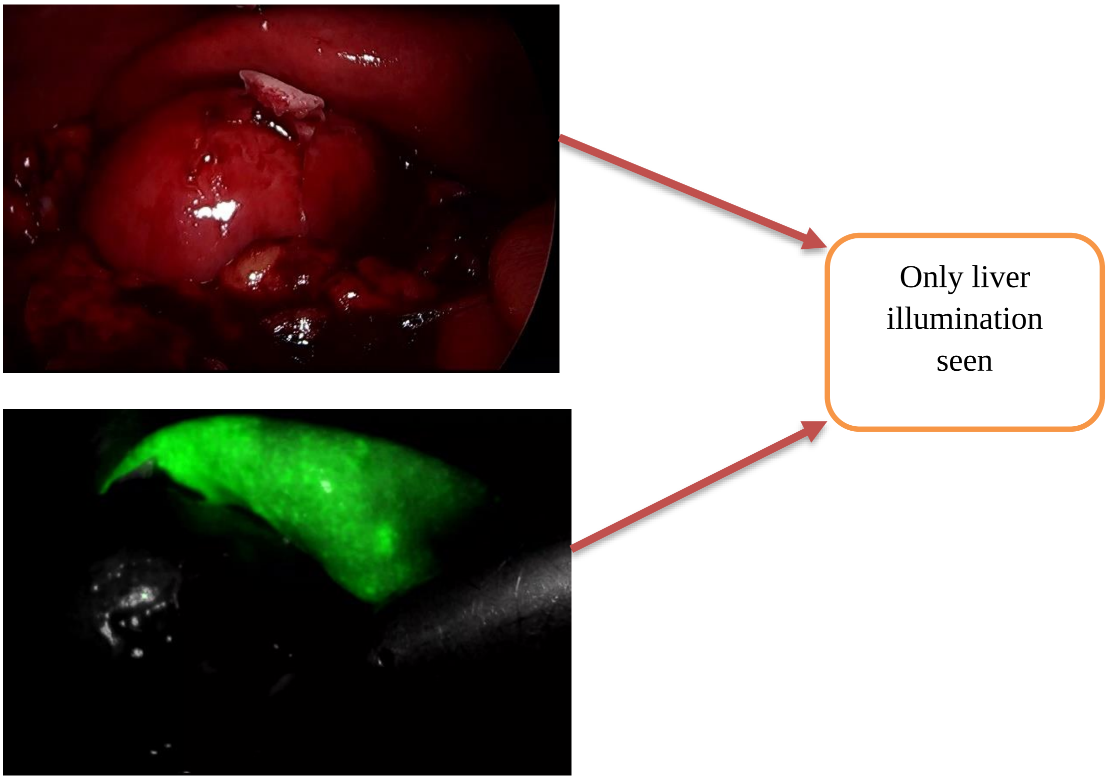


Image 15: Poor Visualization of CBD and CHD in acute edematous cases.

However study conducted by Losurdo et al. have shown contradictory findings suggesting adequate visualization of biliary anatomy even in acute cases, but the exact dosage and time interval was not clearly defined in their study(34)

Similarly in two cases where fluorescence was not visualized severe dense adhesions were noted intraoperatively and hence biliary structures were not visualized. Additional research with a larger sample size is necessary to assess these results. Higher doses or repeated injections of ICG might be required in these cases. This is a significant drawback in the use of ICG since as discussed by Georgiades et al., cases with dense and severe adhesions and inflammation are more likely to have altered biliary anatomy with a higher chance of biliary injury. (35)

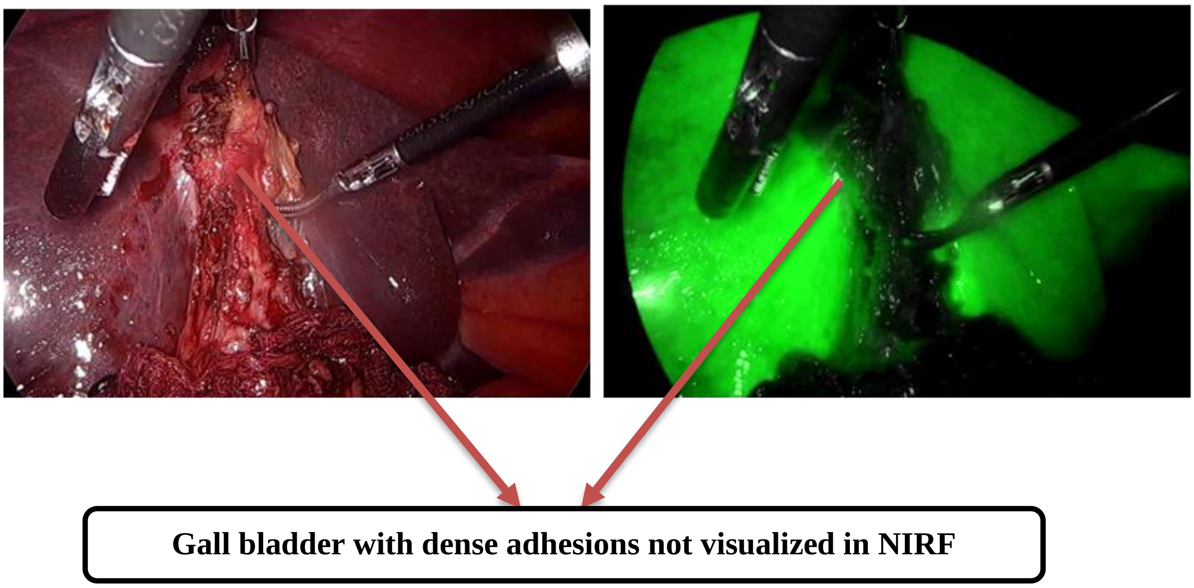


Image 16: Poor Visualization of gall bladder in cases with dense adhesions.

In 2 of the cases, although the dye was given 2 hours prior to the procedure, only liver illumination was identified with almost no illumination of the extrahepatic biliary tree. As explained this could be due to delayed secretion of bile or altered liver function as discussed by Kokudo and Ishizawa, 2012, however, they predominantly focused on hepatic carcinomas. It was observed that albumin levels were comparable in both the groups. Since ICG is bound to albumin it is hypothesized that altered albumin levels can also impact the rate of filtration however, additional investigation is required to comprehend the characteristics of ICG excretion.

The mean length of surgery, the number of post-surgical problems, and the duration of hospital stay did not differ statistically significantly when Ambe et al. examined the operative time between cases with and without the administration of ICG. However, our study showed a statistical significance in the overall mean operative time with a p-value of 0.0003[t] . Similar studies conducted by Broderick et al., showed a significant decrease in the overall operative time, the findings of which were consistent with that of our study.(27) .However the overall operative time can be affected by various factors like amount of intra-abdominal adhesions, drain placement, combining the procedure with another surgical procedure etc., hence rather than the overall time of surgery the time required to identify the critical view of safety can be considered a better parameter to access the effectiveness if the dye.

Studies comparing the time required to attain critical view of safety with the application of ICG have not widely been conducted, despite a substantial body of literature. Few studies have been conducted to identify the overall mean duration of surgery. Koong et al.,Conducted a study to determine the time to attain CVS with ICG, although they found that ICG reduces the time of surgery the overall findings were not statically significant.(36)

These findings were partially corresponding to our study.

Between the two groups, it was observed that there was faster identification of a critical view of safety in cases where the dye was used, which was statistically significant. Thus it is hypothesized that the use of ICG provides a better identification of biliary structures and improves the surgical time.

Additionally, in 20.5% of the cases in the control group, only subtotal cholecystectomy was carried out since the critical view of safety could not be reached and the biliary structures could not be effectively identified. Whereas in the dye group, the CVS was not attained in 11.7% of the cases with 50% of these being in the acute phase. Thus better surgical outcomes were attained in the ICG group. Although these findings were not statistically significant we can hypothesize that better surgical outcomes can be achieved with the ideal use of ICG dye.(37)

A similar observational study conducted Stolz et al, revealed consistent findings with better surgical outcomes and better identification rates of biliary structures with the use of ICG(38,39)

Stolz et al popularized a new term " CVS PLUS" for the identification of CVS with the help of ICG and recommend routine use of ICG in lap Cholecystectomies(38)

In our study also similar findings were noted and similar recommendations can be made. All of the patients did not report any adverse reactions to ICG; these results were in accordance with those of prior trials by Ambe et al. and Boogerd et al (29,30).

Only one case in the control group reported post-operative bile, which further reiterates the importance of ICG. However, this finding was not statistically significant.

Limitations of the study:

1. Single center observational study
2. Further evaluation of the effectiveness of ICG in cases with frozen calots , where the chances of bile duct injury are maximum could not be effectively evaluated
3. Reasons for poor delineation of biliary anatomy in acute cases could not be made out.

CONCLUSION

The use of Indocyanine green in laparoscopic cholecystectomies is effective in successfully identifying the extrahepatic biliary structures including cystic duct, common bile duct and common hepatic duct.

Laparoscopic cholecystectomies performed with the use of Indocyanine green dye, have significantly better and faster delineation of the extra hepatic biliary structures with a much better identification of the common bile duct and , thus improving the overall surgical outcomes by decreasing the operative time and decreasing the risk of bile duct injuries.

SUMMARY

Gall stone disease (cholelithiasis) is a prevalent pathology affecting 10-15% of the population. While many cases are asymptomatic, 1-2% develop symptoms or complications annually, with 20% progressing to symptomatic disease over 15 years. Complications include cholecystitis, cholangitis, choledocholithiasis, gallstone pancreatitis, and rarely cholangiocarcinoma. The etiology of gall stones is multifactorial, involving genetic, dietary, anatomical, metabolic, and pathological factors. The standard treatment for symptomatic cholelithiasis is cholecystectomy, with laparoscopic cholecystectomy (LC) being the gold standard. However, the rise in LC procedures has correlated with an increase in bile duct injuries (BDI), with rates now 0.4-0.6% compared to 0.1-0.2% during the open cholecystectomy era. This rise is attributed to anatomical variations in the biliary tree and the formation of adhesions, complicating the identification of biliary anatomy during surgery.

NIRF-C using Indocyanine Green (ICG) dye has emerged as a technique to visualize biliary anatomy during LC. ICG, when administered intravenously, binds to plasma proteins and fluoresces under near-infrared light is observed, allowing real-time visualization of the biliary tree with special cameras

A prospective, observational study was conducted at Dr. Prabhakar Kore Hospital and Medical Research Center. Participants undergoing LC were divided into two groups: one received preoperative ICG dye and the other did not

ICG dye (AUROGREEN) was administered intravenously 1.5 to 2 hours before surgery.

The dye was reconstituted with sterile water and diluted to a 1:10 concentration.

The procedure was recorded, and the time to identify the critical view of safety (CVS) was measured.

A Stryker 1588 AIM laparoscopic system was used.Patients were monitored for 14 days post-surgery.

The study found that ICG significantly improved the identification of the CBD (67.65%) compared to the control group. The identification rate for the cystic duct was 82.35%, comparable to the control group. However, the ease of identification was better with ICG. The use of ICG reduced the time required to identify the CVS and showed better surgical outcomes with fewer subtotal cholecystectomies performed due to better biliary structure visualization.

ICG fluoroscopy facilitates the identification of biliary structures, thus reducing operative time and the risk of BDI. However, the study noted that in acute cholecystitis cases, ICG fluorescence was less effective due to inflammation and cases with dense adhesions. Higher doses or repeated injections might be required in such cases

Thus the use of Indocyanine green is effective in successfully identifying the extrahepatic biliary structures including cystic duct, common bile duct and common hepatic duct.

Laparoscopic cholecystectomies performed with the use of Indocyanine green dye, have significantly better and faster delineation of the extra hepatic biliary structures with a much better identification of the common bile duct and , thus improving the overall surgical outcomes by decreasing the operative time and decreasing the risk of bile duct injuries.

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ANEXURE 1- – INFORMED CONSENT FORM

"COMPARISON OF LAPAROSCOPIC CHOLECYSTECTOMY WITH AND WITHOUT THE USE OF INDOCYANINE GREEN DYE A 1 YEAR OBSERVATIONAL COHORT STUDY AT A TERTIARY HOSPITAL IN BELAGAVI"

Principal Investigator: BH0121001

Objective: To determine the effectiveness of ICG dye in visualization of the cystic duct, hepatic duct and common bile duct and to evaluate whether earlier identification of critical view of safety can be obtained by using indocyanine green fluoroscopy

Introduction: Gall stone disease is one of the most common pathology encountered in the surgical wards, With 10-15% of the general population suffering from symptomatic or asymptomatic cholelithiasis, which makes it one of the most common pathology of the gall bladder and biliary tree. Laparoscopic cholecystectomy is the most preferred approach for cholecystectomy and is being considered as a Gold standard procedure.However due to frequent and significant variants (about 30%-40%)seen in the biliary tree anatomy,difficulty in clearly identifying the biliary anatomy is a commonly encountered problem faced by surgeons while performing laparoscopic cholecystectomy,which increases the possibilities of dreaded complications like billiary duct injury and post operative bile leak etc.

ICG dye is a novel method used for visualization of biliary tree anatomy during laparoscopic cholecystectomy. Here this study is being undertaken to determine the effectiveness in better visualization of biliary tree anatomy in laparoscopic cholecystectomy.

Explanation of procedure: Pre operatively Indocyanin green dye will be given 1-2hours prior to the procedure intravenously after giving a test dose of 0.1cc.

The patient will undergo routine standard laproscopic cholecystectomy.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: "Name of student/PI, mobile number, email ID" If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "**COMPARISON OF LAPAROSCOPIC CHOLECYSTECTOMY WITH AND WITHOUT THE USE OF INDOCYANIN GREEN DYE A 1 YEAR OBSERVATIONAL COHORT STUDY AT A TERTIARY HOSPITAL IN BELAGAVI"**

". My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

ANNEXURE II - PROFORMA

DATA COLLECTION TABLE			
1	NAME		
2	Patients UHID No		
3	AGE		
4	SEX		
5	HEIGHT		
6	WEIGHT		
7	TYPE OF PROCEDURE		
8	CLEAR VISUALIZATION OF CBD	YES	NO
9	CLEAR VISUALIZATION OF CYSTIC DUCT	YES	NO
10	CLEAR VISUALIZATION OF HEPATIC DUCT	YES	NO
11	IDENTIFICATION OF CYSTIC ARTERY	YES	NO
12	TIME DURATION TAKEN TO ACHIEVE CRITICAL VIEW OF SAFETY		
13	TOTAL TIME OF SURGERY		
14	PREOPERATIVE USG		
15	PREVIOUS HISTORY OF ACUTE CHOLECYSTITIS		
16	CONVERSION TO OPEN		

17	POST OPERATIVE BILE LEAK	

Blood Reports

Si No	Blood Parameters	Values	
1	Hemoglobin		
2	TLC		
3	Sr Creatinine		
4	Total Bilirubin		
5	Direct Bilirubin		
6	SGOT		
7	SGPT		
8	Alkaline Phosphatase		
9	Total protein		
10	Serum Albumin		
11	Serum Globulin		
13	Others		

ANNEXURE III - MASTERCHART

ip no	G dye	age	sex	eight	height in cm	previous history of acute ecystitis	choledocolit iasis	identificatio n of cystic duct	identificatio f CBD	identificatio n of hepatic duct	illumination liver	identificatio n of cystic rtery	total time of rgery	time to identify critical angle of safety	conversion open	type of surgery	post erative e leak	Usg Findings	oglobin	Total ucocyte ount	atelet	Total irubin	Direct irubin	Indirect irubin	GOT	GPT	ALP	protein	lbumin	Mean ation of stay	allergic action
10048091	no	27	female	70	173	no	yes	no	no	no		yes	88	could not be identified.	no	lap subtotal cholecystectomy	no	multiple calculi	12.2	11700	308	1.67	1.12	0.55	63	101	178	6.1	3.7	3	NA
10039715	no	28	male	54	165	yes	no	yes	no	no	-	yes	56	19	no	cholecystectomy	no	single calculi	8.7	9	209	2.03	1.51	0.52	13	20	133	6.5	3.5	3	NA
10028717	no	36	male	63	177	no	no	yes	yes	yes	-	yes	56	24	no	cholecystectomy	no	single calculi 0.8*0.8	13.3	8.4	298	0.57	0.21	0.36	40	30	50	6.9	4.4	8	NA
10030935	no	38	male	87	172	no	no	yes	yes	yes	-	yes	63	23	no	cholecystectomy	yes	single calculi 1.3*2.1cm	14.2	8.7	204	1.42	0.84	0.58	42	22	51	6.2	4	11	NA
10040580	no	40	male	65	173	no	yes	yes	yes	yes	-	yes	84	47	no	cholecystectomy	no	multiple calculi	14.3	6.1	307	0.61	0.26	0.35	33	23	89	8.1	4.8	6	NA
10025020	no	40	female	73	158	no	no	yes	yes	yes	-	yes	88	27	no	cholecystectomy	no	single calculi 0.6*0.2	10.9	7.5	321	0.33	0.14	0.19	20	21	82	7.5	4.2	6	NA
10016799	no	41	female	54	170	yes	no	yes	no	no	-	no	93	45	no	cholecystectomy	no	single calculi 0.7*1.6	13.8	8.9	265	17.5	16.2	1.3	269	190	787	6.2	3.2	6	NA
10023128	no	41	male	75	170	yes	no	yes	yes	yes	-	yes	67	22	no	cholecystectomy	no	single calculi 0.6*1.2	14.5	8.9	340	0.84	0.25	0.59	31	33	100	7	4.2	3	NA
10029229	no	45	female	78	154	YES	no	yes	yes	no	-	yes	86	45	no	cholecystectomy	no	single calculi	9.8	7.2	297	0.18	0.12	0.06	12	17	60	6.3	3.6	4	NA
10027868	no	45	female	83	168	yes	no	yes	no	no	-	no	98	66	no	cholecystectomy	no	single calculi 0.5*0.6	12.2	8.7	279	0.5	0.21	0.29	26	24	199	8	4.7	5	NA
10049447	no	45	male	72	166	no	no	yes	yes	yes		yes	45	24	no	cholecystectomy	no	multiple calculi	16.4	12400	203	0.62	0.13	0.49	37	23	90	7.7	4.5	4	NA
10048145	no	46	female	70	168	no	no	yes	no	no		yes	60	36	no	cholecystectomy	no	single calculi	12.6	7500	268	0.34	0.17	0.17	23	14	97	7.3	4.4	3	NA
10032528	no	47	male	57	174	no	no	no	no	no	-	yes	83	could not be identified.	no	lap subtotal cholecystectomy	no	multiple calculi	15.2	7.5	344	0.65	0.33	0.32	34	26	69	0.5	4.5	4	NA
10018853	no	47	female	62	165	no	no	yes	no	no	-	yes	48	13	no	cholecystectomy	no	multiple calculi with largest 1.1*0.3	12.4	12	267	0.33	0.22	0.11	22	17	98	7.1	4	3	NA
10018788	no	48	female	57	178	no	no	no	no	no	-	no	119	could not be identified.	no	lap subtotal cholecystectomy	no	gb sludge	11.1	7.4	244	0.33	0.23	0.1	14	18	153	8.1	3.9	8	NA
10048065	no	50	male	50	160	yes	no	yes	yes	yes		yes	78	40	no	cholecystectomy	no	multiple calculi	11.2	7400	222	1.34	0.75	0.59	60	34	167	7	4.5	3	NA
10030449	no	51	male	65	166	yes	no	yes	yes	yes	-	yes	76	34	no	cholecystectomy	no	single calculi	9.7	10.8	476	1.2	0.71	0.49	23	21	223	6.7	3.2	3	NA
10046815	no	53	male	45	168	no	no	yes	yes	yes	-	yes	38	12	no	cholecystectomy	no	single calculi 1.3*0.1	12.5	6.4	259	1.05	0.59	0.46	30	39	144	6.6	3.9	3	NA
10042299	no	54	male	58	159	no	no	yes	no	no	-	yes	116	87	no	cholecystectomy	no	single calculi 0.4*0.9	12.5	9.9	251	2.62	1.14	1.48	60	52	115	6	3.8	4	NA
10019264	no	54	male	97	166	no	no	no	no	no	-	no	124	could not be identified.	yes	open subtotal cholecystectomy	no	multiple calculi	14.5	7.9	328	0.41	0.24	0.17	24	36	114	6.8	3.9	8	NA
10031343	no	55	female	78	170	no	no	yes	no	no	-	yes	73	65	no	cholecystectomy	no	single calculi	10.8	21.2	353	0.25	0.04	0.21	25	28	134	4.8	2.4	4	NA
10016081	no	55	male	66	174	YES	no	yes	no	no	-	yes	104	76	no	cholecystectomy	no	multiple calculi with largest calculi 0.4*0.8	10	8.6	243	1.18	0.41	0.77	20	25	62	7.1	4.4	4	NA
10040092	no	56	male	66	164	no	no	yes	yes	yes	-	yes	68	25	no	cholecystectomy	no	single calculi 1*0.7	8.7	3.8	95	0.73	0.44	0.29	26	43	75	6.2	2.8	4	NA
10019381	no	57	male	88	180	yes	no	yes	yes	yes	-	yes	70	36	no	cholecystectomy	no	multiple calculi with largest 1.1*1.8	13.7	12	159	0.7	0.62	0.08	14	22	130	7.1	4	3	NA
10046867	no	58	male	66	176	yes	no	yes	yes	no	-	yes	68	27	no	cholecystectomy	no	single calculi	10.8	10.8	243	1.41	0.61	0.8	18	17	79	6.5	3.9	3	NA
10023559	no	59	female	78	164	yes	no	yes	yes	no	-	yes	72	45	no	cholecystectomy	no	single calculi 0.8*0.5	14.5	8.2	220	0.42	0.22	0.2	16	20	96	7.3	4.2	8	NA
10025789	no	59	female	78	174	no	no	yes	no	no	-	yes	97	51	no	cholecystectomy	no	single calculi 1.3*0.8	12.7	12.6	565	0.56	0.25	0.31	9	22	87	7.8	4	8	NA
10031180	no	63	female	89	162	no	no	yes	no	no	-	yes	45	21	no	cholecystectomy	no	multiple calculi	13.7	5.6	241	0.43	0.17	0.26	13	24	74	6.8	4.2	5	NA
10032327	no	63	female	74	166	yes	no	yes	yes	yes	-	yes	78	23	no	cholecystectomy	no	single calculi	6.9	11	272	0.29	0.12	0.17	14	26	88	7.5	4.4	6	NA
10027693	no	64	male	91	180	no	no	no	no	no	-	no	107	could not be identified.	no	lap subtotal cholecystectomy	no	single calculi 0.4*0.9	13.1	6.1	159	1.88	0.93	0.95	16	29	62	8	4.3	4	NA
10047371	no	64	male	69	158	no	no	yes	no	no	-	yes	53	28	no	cholecystectomy	no	multiple calculi	12	7600	217	0.46	0.21	0.25	11	18	39	7.1	4.6	3	NA
10062169	no	64	female	65	156	yes	yes	yes	no	no		yes	98	could not be identified.	no	lap subtotal cholecystectomy	no	single calculi	10.5	7900	268	0.52	0.8	0.4	19	28	92	7	3.8	7	NA
10030023	no	65	male	67	168	yes	no	no	no	no	-	yes	87	32	no	cholecystectomy	no	single calculi	13.4	5	233	1.32	0.76	0.56	45	19	57	5.9	3.8	4	NA
10029579	no	73	male	84	166	yes	no	no	no	no	-	yes	45	could not be identified.	no	lap subtotal cholecystectomy	no	multiple calcul 0.8*1.1	11	6.6	226	0.39	0.18	0.21	12	18	75	7.2	4.2	5	NA

'P NO	G dye	age	sex	eight	eight	previous history of cute cystitis	ocolithi asis		identification ic duct NIRF	identification BD with NIRF	identification of hepatic t with NIRF	illumination of r with NIRF	identification of cystic ry with NIRF	time of rgery	time to identify al angle afety	sion to pen	post ive bile leak	type of surgery performed	Usg Findings	globin	Total cocyte ount	telet	ilirubin	Direct irubin	direct rubin	GOT	GPT	ALP	rotein	lbumin	duration stay	lergic action
10036505	yes	22	female	67	168	no	no		no	no	no	yes	YES	52	31	no	no	cholecystectomy	single calculi	13.7	7100	544	1.8	0.9	0.9	30	47	131	7	3.2	4	nil
1149365	yes	25	female	56	167cm	no	no		yes	yes	yes	yes	yes	61	34	no	no	cholecystectomy	multiple calculi 1.1*08mm	10	6700	231	0.44	0.16	0.28	23	15	60	6.9	4.1	4	nil
1177782	yes	25	female	66	160	yes	no		yes	yes	yes	yes	yes	60	23	no	no	cholecystectomy	cholecystoduodenal fistula	15.7	7400	220	0.97	0.33	0.64	21	19	45	7.8	4.8	7	nil
1183823	yes	26	male	81	174	no	no		yes	yes	no	yes	yes	43	29	no	no	cholecystectomy	sinle calculi 1.4*0.6 cm	15.7	7400	257	0.64	0.26	0.38	20	24	79	7.1	4.4	3	nil
1197032	yes	26	female	67	146cm	yes	no		no	no	no	yes	no	32	could not be	yes	no	open subtotal-cholecystectomy	multiple calculi	12.3	9200	183	0.67	0.33	0.34	34	32	87	7.2	4.6	8	nil
1138404	yes	27	female	68	153	no	no		yes	yes	yes	yes	yes	68	14	no	no	cholecystectomy	post ercp with multiple calculi	11	6700	105	0.86	0.35	0.51	18	17	118	6.5	3.4	4	nil
10012707	yes	27	female	69	159cm	no	no		yes	yes	yes	yes	yes	60	24	no	no	cholecystectomy	single calculi	14	8900	312	0.29	0.1	0.19	27	22	80	6.7	3.7	5	nil
10003531	yes	28	female	56	158	no	no		yes	yes	yes	yes	yes	38	24	no	no	cholecystectomy	multiple calculi 4*6mm	14.4	7600	240	2.04	0.92	1.12	74	112	113	8.1	4.6	7	nil
10032585	yes	32	female	67	168	yes	no		yes	yes	yes	yes	yes	65	18	no	no	cholecystectomy	single calculi 1.1*0.8 cm	12.8	8800	212	0.46	0.22	0.24	22	30	134	7.1	4.1	3	nil
1199838	yes	34	female	76	160cm	no	no		no	no	no	yes	yes	75	could not be	no	no	laparoscopic subtotal-	multiple calculi	12.8	8100	273	0.2	0.03	0.17	23	26	76	6.7	4	4	nil
1178934	yes	35	female	65	159cm	no	no		yes	no	no	yes	YES	58	21	no	no	cholecystectomy	single solitary calculi	10.8	6100	266	0.6	0.3	0.3	45	66	80	7.8	4.8	4	nil
1171959	yes	36	male	70	162cm	no	no		yes	yes	yes	yes	yes	38	7	no	no	cholecystectomy	single calculi	11.2	8700	234	0.64	0.45	0.19	34	44	117	7.2	4,.4	3	nil
10025228	yes	38	male	70	174	no	no		yes	yes	no	yes	yes	83	35	no	no	cholecystectomy	multiple calculi	11.7	6400	269	0.18	0.11	0.09	20	13	82	7	4.3	3	nil
1153301	yes	40	male	76	167	yes	no		yes	no	no	yes	YES	48	34	no	no	cholecystectomy	multiple calculi with largest 1.1*1.6	12.7	9200	338	0.34	0.13	0.21	16	21	101	7	4.5	3	nil
10025020	yes	40	female	72	160cm	no	no		yes	yes	yes	yes	yes	40	11	no	no	cholecystectomy	single calculi 1.1*0.8	11	7600	298	0.9	0.5	0.4	14	35	170	7.1	3.4	3	nil
10023128	yes	41	male	78	166cm	no	no	acut e	no	no	no	yes	no	88	could not be	no	no	laparoscopic subtotal-	acute cholecystitis with multiple calculi	12.1	17000	211	0.89	0.5	0.39	45	34	130	6.8	4	7	nil
1163731	yes	45	female	72	159	yes	no		yes	yes	yes	no	yes	70	54	no	no	cholecystectomy	multiple calculi with thickened gb wall	11.4	6100	198	0.28	0.11	0.17	32	42	93	7.3	4.2	4	nil
1200600	yes	45	male	48	151	yes	no		yes	yes	yes	yes	yes	56	17	no	no	cholecystectomy	single calculi 1.3*08cm	13.5	9900	222	0.75	0.33	0.42	20	10	90	6	3.6	3	nil
10042057	yes	46	female	67	155cm	no	no		yes	yes	no	yes	yes	45	19	no	no	cholecystectomy	multiple calculi 7*6mm	12	7250	202	2.74	1.94	0.8	108	49	118	5.1	2.65	3	nil
10018853	yes	47	female	70	161	no	no		yes	yes	yes	no	yes	36	2	no	no	cholecystectomy	single calculi 1.1*09 cm	12.4	12000	267	0.33	0.22	0.11	17	22	98	7.1	4	3	nil
1174986	yes	50	male	79	170	yes	no		yes	yes	no	yes	yes	70	21	no	no	cholecystectomy	multiple calculi	12.8	5600	213	0.59	0.25	0.34	17	18	82	7.6	4.4	4	nil
1163734	yes	50	female	65	157	yes	yes		yes	no	no	no	YES	87	38	no	no	cholecystectomy	multiple calculi	12	6600	297	0.38	0.14	0.24	20	10	112	7.8	4.8	3	nil
1209207	yes	54	male	80	178cm	no	no	acut	no	no	no	no	YES	66	45	no	no	cholecystectomy	cholelithiasis 1.2*1cm	8.3	17.5	565	2.5	1.2	1.3	15	14	34	6.9	4.7	11	nil
1149476	yes	55	male	56	167cm	yes	yes		yes	yes	yes	yes	yes	41	27	no	no	cholecystectomy	multiple calculi, largest 6.9*3*5 with bowel wall oedematous	12.1	7000	253	0.76	0.1	0.66	42	20	208	7.3	4.1	3	nil
10014057	yes	55	female	62	154cm	no	no		no	no	no	no	no	65	could not be	no	no	laparoscopic subtotal-	post ercp with multiple calculi	11.3	8000	169	0.52	0.2	0.32	37	24	107	7.7	4.3	5	nil
10035529	yes	58	male	68	155cm	yes	yes		yes	no	no	no	yes	86	23	no	no	cholecystectomy	multiple calculi	12.1	15700	246	0.44	0.21	0.23	20	10	75	7.4	4.5	5	nil
11177703	yes	60	female	82	173	yes	no		yes	yes	yes	yes	yes	68	13	no	no	cholecystectomy	single calculi 1.3*08cm	13.9	11700	310	0.34	0.26	0,8	17	15	75	6.6	4.2	4	nil
10023021	yes	60	female	82	156cm	yes	no		yes	yes	yes	no	yes	83	21	no	no	cholecystectomy	single calculi	11.4	7200	401	0.69	0.24	0.45	16	13	55	7.7	4.6	4	nil
10004137	yes	65	female	70	160	yes	no		yes	yes	yes	yes	yes	18	4	no	no	cholecystectomy	Multiple Calculi, largest 8mm*6mm	13.8	10,000	358	0.88	0.36	0.52	50	52	146	7.8	4.7	3	nil
10045098	yes	65	female	70	160	yes	no		yes	yes	yes	no	yes	54	28	no	no	cholecystectomy	multiple calculi 6*6mm	12.3	7400	226	0.23	0.1	0.13	16	14	65	7	4.2	4	nil
10035648	yes	67	female	70	164	yes	no		yes	yes	yes	yes	yes	45	23	no	no	cholecystectomy	cholelithiasis with choledocolithiasis	14	5290	179	0.46	0.19	0.21	17	13	78	7.5	3.9	8	nil
1200313	yes	68	female	56	154	yes	no		yes	yes	yes	no	yes	56	22	no	no	cholecystectomy	single calcu;l of 1.2cm	14.5	8900	340	0.84	0.25	0.59	33	31	100	7	4.2	3	nil
1163082	yes	70	male	68	168cm	no	no		yes	no	no	no	yes	78	45	no	no	cholecystectomy	multiple calculi	11.2	8600	301	1.07	0.6	0.47	23	25	152	6.7	3.7	6	nil
10044834	yes	78	male	75	168	yes	no		yes	yes	yes	yes	YES	54	19	no	no	cholecystectomy	single calculi	13.6	5800	326	0.74	0.19	0.55	21	12	76	7.8	4.7	4	nil