30 Day outcomes of 1000 consecutive Laparoscopic Cholecystectomies across four Cape Metropole hospitals in Cape Town

by

Maahir Kariem
KRMMAA001

Submitted as a minor dissertation in partial fulfilment of the requirements for the degree

MASTER of MEDICINE (MMed) in SURGERY

Department of Surgery - Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

University of Cape Town

Supervisor: **A/Professor Christo Kloppers**

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

University of Cape Town

Declaration

I, **Maahir Kariem**, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signed by candidate

Signed: M Kariem

Acknowledgements and Dedications

There are many to whom I owe my sincere gratitude and thanks for their contributions and support in order to complete this manuscript.

First and foremost, I thank my Almighty Allah for granting me this life and for blessing me with the ability to help people.

To my supervisor:
Professor Christo Kloppers for your guidance, mentorship and encouragement throughout my research time which has made this study and manuscript possible.

To my first Surgical Mentor:

Dr Ferhana Gool. I owe my professional career to you. You are an inspiration to all of us who have been guided by your abled hands and selfless heart.

I dedicate this thesis to my parents, Gilmie and Sharifa. I will never be able to repay you for the life you have afforded me. Thank you for the timeless efforts you have given me to this day, for the values you have instilled in me and for your unconditional love.

Finally to my wife Mishka and children Umr and Qasim. Thank you for your unwavering support, patience and steadfastness in allowing me to pursue my dream. I will never be able to make up for the time lost, but I do this for you.

Table of contents

Part A: Publication ready manuscript

Title Page	pg. 5
Abstract	pg. 6
Article	pg. 7
References	pg. 29

Part B: Supporting documents

Abbreviations	pg. 33
Index of tables	pg. 34
Author guidelines of World Journal of Surgery	pg. 35
Departmental Research Committee Approval	pg. 38
Human Research Ethics Committee Approval	pg. 39

Part A – Publication ready original manuscript

30 Day outcomes of 1000 consecutive Laparoscopic Cholecystectomies across four Cape Metropole hospitals in Cape Town

M Kariem[1], F Gool[1,3], N Kariem[1], N Karimbocus[1], JC Kloppers[1,2]

[1] University of Cape Town Faculty of Health Sciences, Division of General Surgery, Groote Schuur Hospital, Cape Town, South Africa
[2] Hepatobiliary Unit, Groote Schuur Hospital, Cape Town, South Africa
[3] General Surgery Unit, Mitchells Plain Hospital, Cape Town, South Africa

Corresponding Author: Dr Maahir Kariem, Division of General Surgery, Groote Schuur Hospital, University of Cape Town Faculty of Health Sciences, Observatory, Cape Town, South Africa, macateen@gmail.com, +27826640743

Short Title: Laparoscopic Cholecystectomy, Cape Town Metro West

Key words: Laparoscopic Cholecystectomy, Outcomes

The authors declare that they have no conflict of interest.

Informed consent was obtained from all individual participants included in the study

This manuscript was presented as a podium presentation at the Fifteenth biennial congress of the European-African Hepato-Pancreato-Biliary Association in Lyon, France on the 9th of June 2023

Abstract

Background: Laparoscopic Cholecystectomy (LC) is the standard of care for symptomatic gallstone disease. It has a steep learning curve and can associated with significant post operative morbidity and mortality.

LC carries a morbidity of 1.6 – 5.3%, mortality of 0.05 – 0.14% and readmission rates of 3.3% (0-11.7%). We aimed to evaluate the 30 day outcomes of LC across four metropole hospitals in the Western Cape (WC) including mortality, length of stay, readmissions and complications according to the Clavien-Dindo Classification system.

Methods: A retrospective review of a prospective database was performed. The data collection was collected between September 2019 and July 2022. Relative clinical, operative findings and post operative outcomes were analysed.

Results: There were 1000 consecutive LC included in this study. The mean post operative length of stay was 1.92 days. Fifty-one patients developed surgical complications of which the most common surgical complication was a bile leak (n = 14) and intra-abdominal collections (n=11). Seven patients with bile leaks required reintervention. Four (0.4%) bile duct injuries (BDI) were reported in our series. Twenty-five percent of post operative complications were graded Clavien-Dindo IIIa and 28% were graded Clavien-Dindo IIIb. The 30 day readmission rate was 3.8% (n=38). Thirty-five surgical complications were noted of which 22 (62.8%) required reintervention. There were three reported mortalities (0.3%).

Conclusion: Laparoscopic Cholecystectomy is considered the standard of treatment for gallstone disease and has potential serious complications. Our outcomes reported in this series is similar to that of other studies.

Introduction

Gallstone disease is one of the most commonly encountered diseases in general surgical practice [1] and carries a global incidence of between 10-20% [2]. Laparoscopic cholecystectomy (LC) since its introduction in the late 1980's has grown quickly in its acceptance and is now the standard treatment for symptomatic gallstone disease [3]. It however remains a procedure with an inherent steep learning curve with potential for serious complications [1].

The technique of a LC is probably one of the most significant major surgical advances since its inception. The advantage of the laparoscopic approach includes less post-operative pain, shorter hospital stay, faster recovery, improved cosmetic result, early return to work and fewer complications such as surgical site infections, adhesions and operative time [4].

Despite the advances of laparoscopy, it is reported that there is up to a fivefold increase in the rates of bile duct injuries (BDI) with individual reports suggesting BDI rates between 0.2 - 1.5% compared to the open procedure with BDI rates generally accepted between 0.1 - 0.2% [2,3]. Other major risks of LC include major vascular injury, biliary leak and cautery injuries [2].

Over 750 000 LC are performed in the United States of America (US) and 50 000 in the United Kingdom (UK) annually [5]. Indications for surgery include colic, cholecystitis, cholangitis, pancreatitis, choledocholithiasis and gallbladder polyps [1]. Literature suggests that 90% of elective and 70% of emergency cholecystectomies

are performed laparoscopically. LC carries a morbidity of 1.6-5.3% and a mortality of 0.05-0.14% [2].

Readmission rates following a LC is 3.3% (0 - 11.7%) [5]. The causes of readmission ranges from post operative pain, nausea and vomiting to major surgical complications such as bile duct complications, intra-abdominal collections, haemorrhage and wound sepsis, as well as medical complications related to the cardiovascular and respiratory systems. Surgical complications slightly outweigh medical complications [3,5-7].

By far, the highest risk of readmission occurs within the first post operative week. In a study performed on ambulatory LC, 11.1% of patients were admitted within the first 24 hours and 53.3% of patients were readmitted within the first seven days [7].

Unanticipated hospital admission within 30 days of surgery are important measures of quality of care. It relates to both the inconvenience to the patients as well as to cost, resources utilization and associated morbidity and mortality [5].

A similar local study performed reported an overall complication rate of 16.2% in a study population of 210 patients, with complication rates being similar to other international published series [8].

Although a very common procedure there is a paucity of South African data published on the outcomes of LC.

Methods

A retrospective analysis of a prospectively maintained ethics approved (HREC: R040/2019) database was performed. The database was initiated in September 2019 and the population sample number needed for this study was reached in July 2022. Data was collected on a standard proforma checklist and operative note and entered into the database using the secure, web-based Research Electronic Data Capture (REDCap) tool hosted at the University of Cape Town (UCT) [9,10]. The checklist and operative note was based on a previously published checklist by Connor et al (2014). This checklist and operative note included information on patient characteristics, indication for LC, patient co-morbidities, pre-operative investigations and intra-operative checklists, procedural details and final comments. Patient follow up included length of stay, surgical and non-surgical complications and interventions required. 30 day readmissions were determined using the Electronic Continuity of Care Record (ECCR), the Western Cape Government Health website displaying patient's admissions, hospital stays and discharges.

A review of readmissions was conducted using the National Health Laboratory Service (NHLS) for blood investigations, Picture Archiving and Communication System (PACS) for radiological investigation or intervention, discharge summaries on ECCR or folder reviews at the relevant participating hospitals. Post operative complications and readmission at 30 days were graded using the Clavien-Dindo Classification system [11].

Inclusion Criteria included all LC in patients 18 years and older. All intended open, oncological and cholecystectomies as part of another operation i.e. trauma or pancreaticoduodenectomy were excluded.

Privacy and Confidentiality

Patients were included in the database according to the previously determined HREC requirements for written informed consent, which includes the possibility of using data from the database in future studies, therefore a separate informed consent for this study was not required. The REDCap database is a secure, password protected database. All data was exported without patient identifiers for the purpose of analysis to ensure that patient confidentiality is maintained. Exported data was stored electronically on a password protected computer. Only authors of the manuscript had access to the REDCap database and any electronic or hard copy forms of extracted data.

Funding

This research did not receive any grant from funding agencies in the public, commercial or not-for-profit sectors

Statistical Analysis

Numerical values where used for the different variables used. Where applicable percentages were assigned to numerical values. Furthermore, some data was summarised as median with interquartile range or frequency and percentage for non-parametric continuous and categorical data respectively.

Results

Patient demographics and clinical characteristics

This data series analysed 1000 consecutive LC performed in the Cape Metropole during the study period of which 850 (85%) were female and 150 (15%) were male with a mean age of 41 years. A total of 392 (39.2%) patients had associated comorbidities with cardiovascular disease being the most common (n=236). The most common American Society of Anaesthesiologist (ASA) classification was physical status II with 457 (51.8%) patients. There were no ASA IV or V patients. The mean Body Mass Index (BMI) was 32.47 kg/m^2. A total of 57 (6.2%) patients were documented to be Human Immunodeficiency Virus (HIV) positive however in 590 patients the HIV status was not recorded.

Of the 1000 LC performed, 707 (70.7%) LC were performed on an elective basis and 293 (29.3%) were performed on the same admission. The most common indication for LC was acute cholecystitis (n=338), followed by biliary colic (n = 309), choledocholithiasis (n=184) and gallstone pancreatitis (n=149). The remaining 20 patients had LC for other indications which included Mirizzi syndrome (n=6), gallbladder polyps (n=4), gallbladder empyema (n=3), cholangitis (n=3), adenomyomatosis (n=1), acalculous cholecystitis(n=1), cholecystoduodenal fistula (n=1) and recurrent biliary sepsis (n=1).

Thirty-six percent of LC were performed at a tertiary academic hospital while 64% LC were performed at secondary or district level hospitals. Of note, all four participating institutions are public sector hospitals.

LC was the final procedure performed in 907 (90.7%) of the cases and 84 (8.4%) laparoscopic subtotal cholecystectomies (LSC) were performed of which 69 (83.1%)

were fenestrating LSC and 14 (16.9%) were reconstituting LSC. One gallbladder was left in situ and eight procedures were converted to open.

Seventy-three percent of females had an elective LC and 27% had a same admission LC. Fifty-nine percent of males had an elective LC and 41% had a same admission LC. The most common indication for the female population was biliary colic (n=271, 31.9%) and acute cholecystitis in males (n=38, 25.3%). Table 2 illustrates indications for males and females and the timing of surgery.

There were a total of 64 reported complications in 51 patients. Fifty-two (81.3%) surgical and 12 (18.7%) non-surgical complications were noted. Eight patients had more than one surgical complication and five patients had associated non-surgical complications. Complications are illustrated in table 3.

Bile leaks

There were 14 reported bile leaks of which 10 were female and four were male. Eight patients were undergoing LC for acute cholecystitis, three for gallstone pancreatitis and three for choledocholithiasis. Of the 14 bile leaks reported, LC was the final procedure in five cases. A subtotal cholecystectomy was performed in eight of the cases and one open subtotal cholecystectomy was performed. Seven patients required reintervention. Six patients required re-operation, two of which required an additional Endoscopic Retrograde Cholangiopancreatography (ERCP) and one required an additional percutaneous drainage. One patient required an ERCP and percutaneous drainage.

Three patients who had a bile leak were readmitted within 30 days. Two patients were admitted with intra-abdominal collections. The first patient treated with antibiotics and the second treated with percutaneous drainage. The third re-admission presented with an upper gastrointestinal bleed secondary to warfarin toxicity.

Bile Duct Injuries

There were four reported BDI in this series. All four cases were elective admissions for LC. In two cases the indication was acute cholecystitis, one biliary colic and one choledocholithiasis. Of the four BDI, two patients underwent LSC, one LC was performed and one procedure was converted to open. In three of the cases a BDI was identified immediately. Two of these cases were classified as Strasberg D. One was primarily repaired and the other managed conservatively with an intra-operatively placed drain. The third case was converted to an open procedure with an immediate hepaticojejunostomy for a Strasberg E1 injury. The fourth case was a delayed diagnosis and was managed with a delayed open hepaticojejunostomy. Of the four BDI, one patient was readmitted with an intra-abdominal collection which was managed with antibiotics.

Intra-abdominal Collection

There were 11 intraabdominal collections reported. Four of the LC were performed electively and seven on the same admission. LC was the final procedure performed in six of the cases and a LSC in five of the cases. Six patients required

reintervention. Two patients required reoperation and an ERCP, one patient required and ERCP and a percutaneous drain and one patient required a percutaneous drain and an ERCP. One patient was managed with an ERCP alone and the other with a percutaneous drain.

Intra-abdominal bleeding

In our series, three patients complicated with intra-abdominal bleeding. LC was performed in one of the patients and a LSC in the remaining two. Two patients required re-operation and one patient managed conservatively.

Jaundice

Two patients presented with jaundice post operatively and both were treated with an ERCP with subsequent clearance of the common bile duct (CBD) of stones. The first patient underwent a LC for cholelithiasis and the second patient underwent a subtotal cholecystectomy for choledocholithiasis. The second patient had had a preoperative ERCP with stone extraction.

Wound Complications

Four patients developed wound complications. Three patients developed wound infection and the other a wound haematoma. Two patients required re-operation and the other two were managed conservatively with antibiotics.

Bowel Injury

There were two bowel injuries reported. Both patients were undergoing elective LC. The first bowel injury was a female undergoing a LC for choledocholithiasis who sustained a colonic injury. This procedure was converted to an open right hemicolectomy and primary anastomosis. The second bowel injury occurred in a male patient undergoing a LC for biliary colic who sustained a small bowel injury which was primarily repaired laparoscopically.

Other

Retained stones accounted for nine of the complications of which eight required post operative ERCP. The other documented complications included an ileus and post operative pain in two patients. Four procedures were done electively and eight on the same admission.

Non-surgical complications

There were 12 reported non-surgical complications. Four patients were admitted electively and eight same admission procedures were performed. Of these 12 patients, five patients had associated surgical complications.

Complications were mostly graded Clavien-Dindo IIIa (n = 16) and IIIb (n = 18). There were two mortalities in the perioperative period.

The first, a 29 year old male undergoing a same admission LC for choledocholithiasis and mild cholangitis. A LC was performed and had an on table ERCP where the CBD was cleared of two stones. He was morbidly obese and suffered a cardiac arrest on post operative day 1 due to a myocardial infarction based on an elevated Troponin level done at the time of the cardiac arrest. The second patient was a 47 year old female who underwent an elective LC for biliary colic who was deemed not a candidate for the intensive care unit (ICU) on the basis of her significant cor pulmonale who subsequently had worsening post operative renal and respiratory failure. She demised on post operative day 5.

Thirty-eight patients in our series were admitted within 30 days after being discharged. Thirty (78.9%) patients were female and eight (21.1%) patients were male. Sixteen (42.1%) cases were performed electively and 22 (57.9%) were performed on the same admission. The most common indication for LC in those patients who were readmitted was choledocholithiasis (n=11), gallstone pancreatitis (n=9) and acute cholecystitis (n=9). LC was the final procedure in 31 cases, eight patients had a LSC and one patient had an open procedure. Five patients had had a previous surgical or non-surgical complication. There were 43 documented complications in the 38 patients readmitted of which 37 (86%) were surgical complications and six (14%) were non-surgical complications. The most common indications for readmission were intraabdominal collections (n=9), post operative pain (n=7), bile leak (n=6) and retained stones (n=6). In all, 22 (62.8%) patients required reintervention. Of the documented readmissions, 14 (36.8%) patients were Clavien-Dindo grade IIIa. There was one mortality, a 74 year old female who had undergone a same admission subtotal cholecystectomy for recurrent biliary sepsis.

She was discharged on post operative day 3. She was subsequently readmitted on post operative day 4 in septic shock. She was reoperated on immediately but was overcome by her overwhelming septic shock and demised within 12 hours of her reoperation in the ICU.

Table 1 . Demographic characteristics of patients undergoing laparoscopic cholecystectomy in the Cape Metro West Region from September 1, 2019 through July 31 2022.

Variables	Laparoscopic Cholecystectomy N = 1000 (%)
Demographics	
Female Male	850 (85%) 150 (15%)
Age in years, median (IQR)	43 (34 – 56)
BMI, median (IQR)	31 (27 – 37)
Comorbidities	
Cardiovascular	237 (23.7%)
Respiratory	62 (6.2%)
Liver	9 (1%)
Diabetes	86 (8.6%)
Retroviral disease*	57 (5.7)
Other	112 (11.2%)
ASA	
ASA I ASA II ASA III ASA IV ASA unknown	376 (42.6%) 457 (51.8%) 50 (5.7%) 0 (0%) 117 (11.7)

*590 patients with unknown HIV status

IQR -Interquartile range, BMI – body mass index, ASA – American Society of Anaesthesiologists

Table 2. Indications for patients undergoing laparoscopic Cholecystectomy according to gender and admission type from September 1 2019 through July 31 2022

Indication	**Female (n =850)**		**Male (n = 150)**		**Total**
	Elective	Same Admission	Elective	Same Admission	
Biliary Colic	271	17	20	1	309 (30.9%)
Cholecystitis	198	78	38	24	338 (33.8%)
Choledocholithiasis	98	53	16	17	184 (18.4%)
Gallstone Pancreatitis	47	78	11	13	149 (14.9%)
Other	5	5	3	7	20 (2%)
Total	619 (72.8%)	231 (27.2%)	88 (58.7%)	62 (41.3%)	1000

Table 3. Surgical and non-surgical complications from patients undergoing laparoscopic cholecystectomy in the Cape Metro West from September 1 2019 through July 31 2022

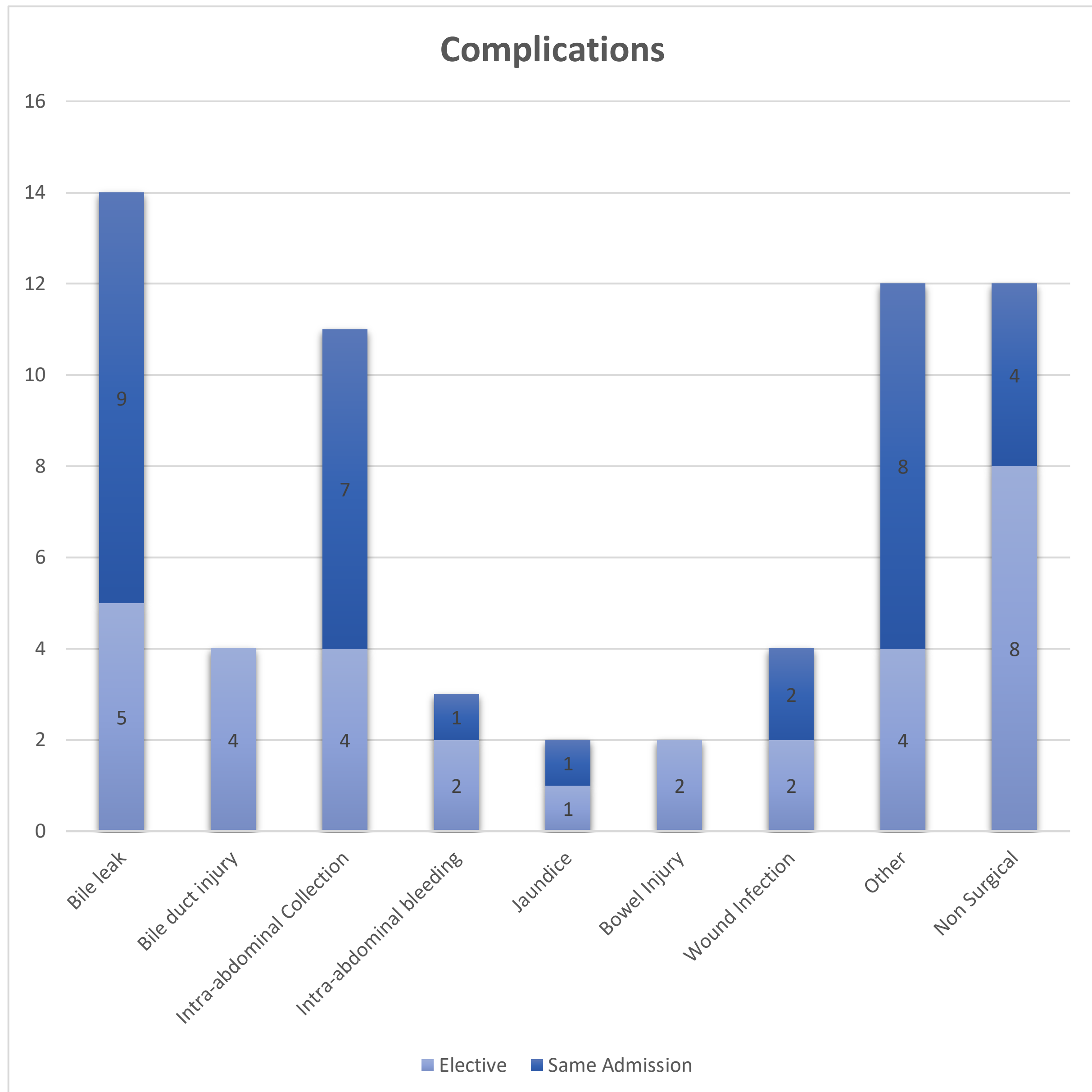


Table 4. Clavien-Dindo grading per complication for patients undergoing Laparoscopic Cholecystectomy from September 1 2019 through July 31 2022

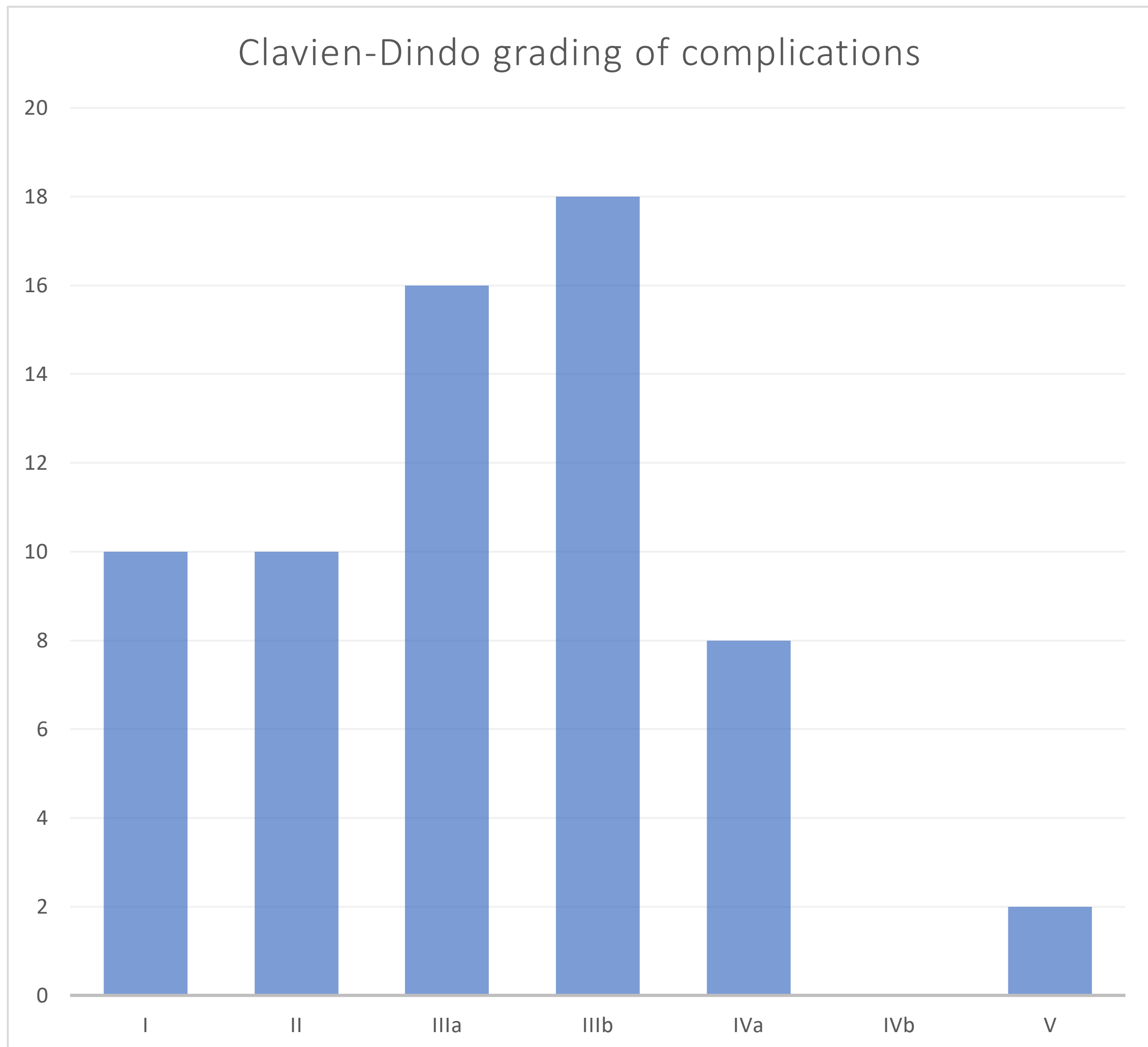


Table 5. Readmissions for patients undergoing Laparoscopic Cholecystectomy from September 1 2019 through July 31 2022

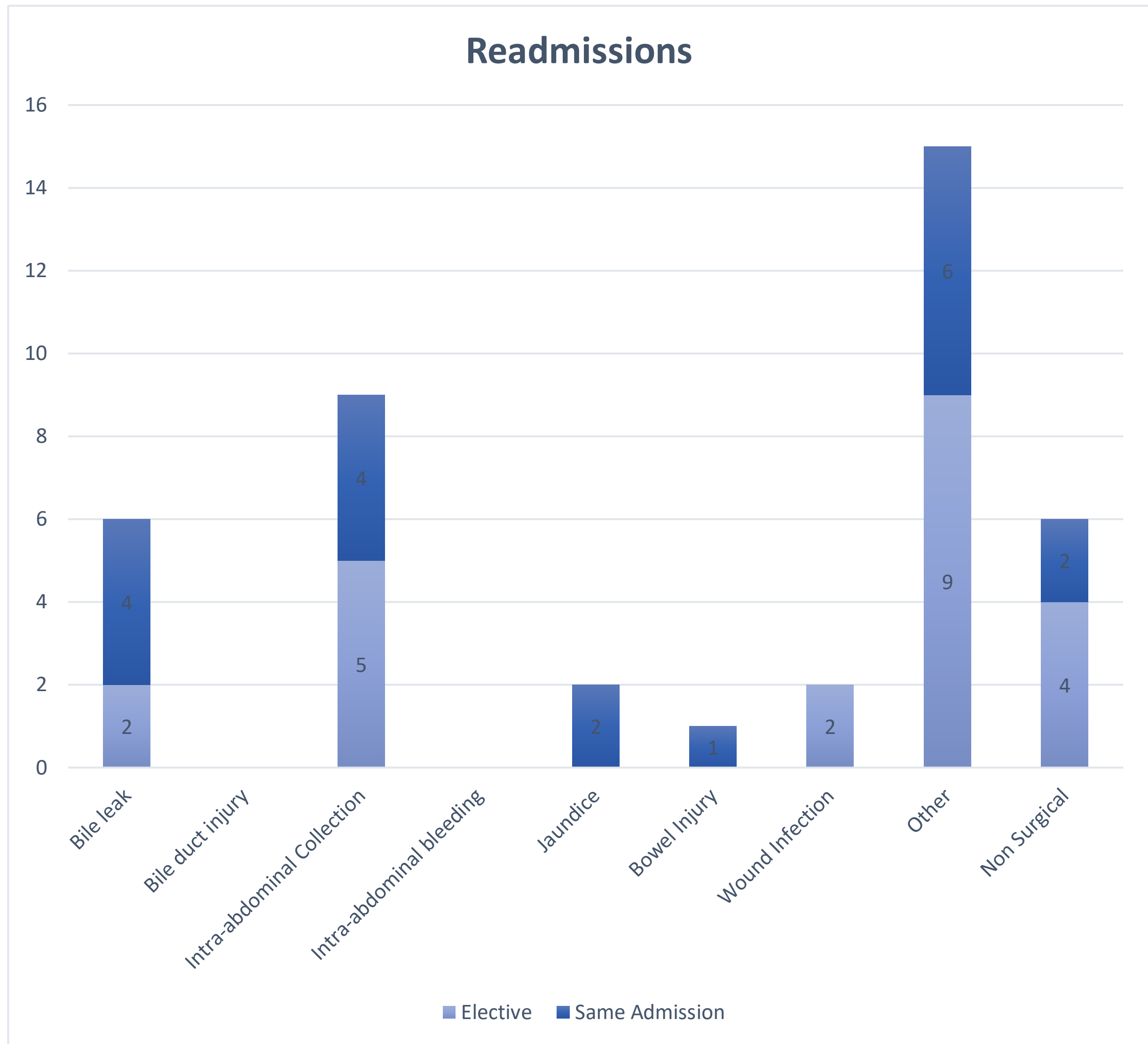
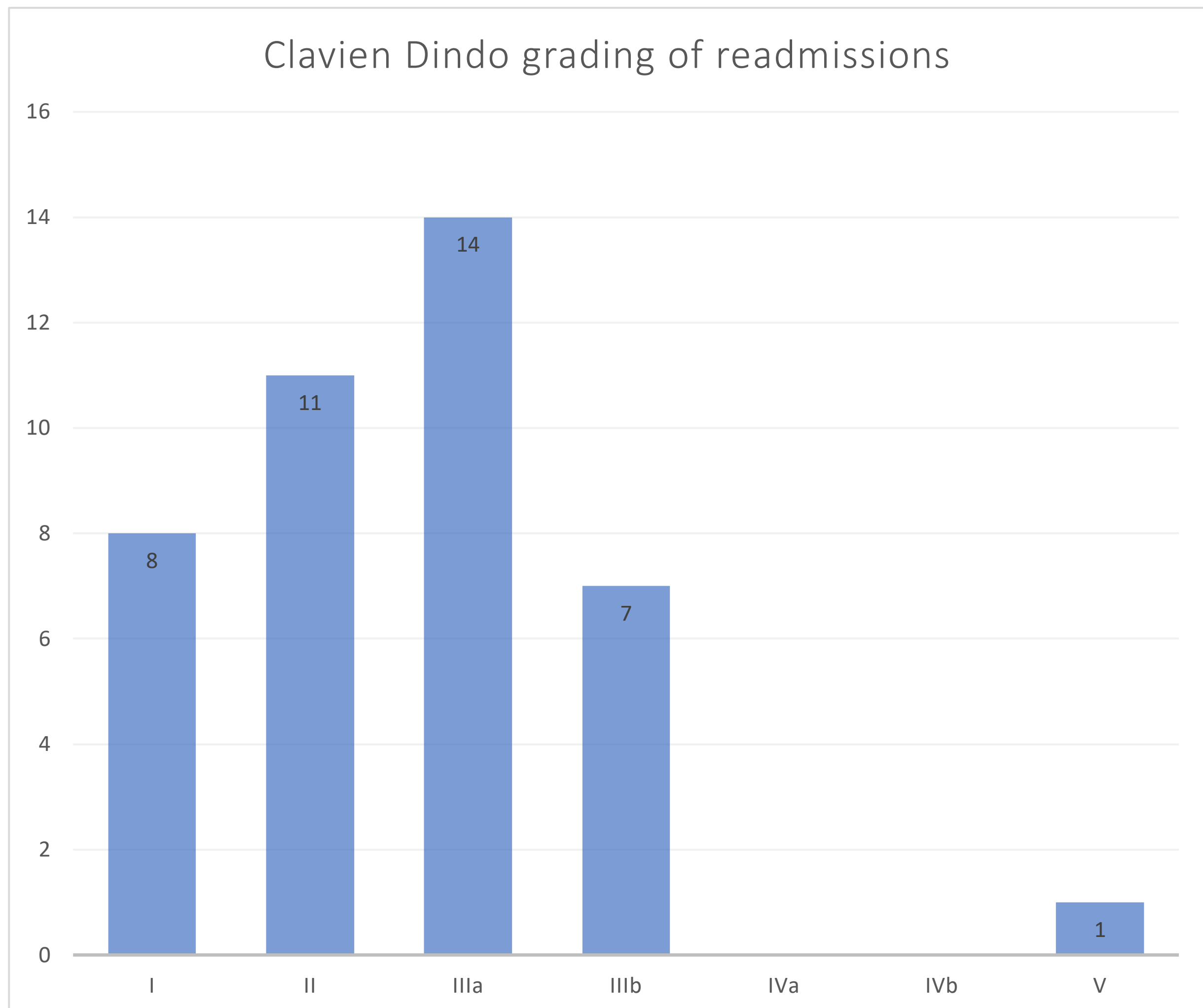


Table 6. Clavien-Dindo grading for readmissions per complication for patients undergoing Laparoscopic Cholecystectomy from September 1 2019 through July 31 2022



Discussion

LC represents a significant change in the management of gallstone disease. Not only is it the most commonly performed operation on the digestive tract, but considered the standard of care for gallstone disease [12].

The advantages of LC are less postoperative pain, shorter hospital stay, faster recovery, improved cosmetic results, early return to work, fewer complications such as infection, adhesions, shorter operating time [13] and it is superior to other developed techniques because of economic advantage [14].

In a recent published locally study, there has been a 92% increase in the rate of cholecystectomies in South Africa over the past 10 years. This has been ascribed to changes in risk factors such as dietary changes and an increasing BMI resulting in an increased incidence of gallstone disease, coupled with a lower threshold for surgery and a lower morbidity associated with LC [15].

Of the 1000 LC reported in this series, 85% of LC were performed on female patients. The median age of 41. 39.2% of patients had associated co morbidities, the median BMI was 32.47 kg/m^2 and 93% of patients had a preoperative ASA I/II. Published data from a similar developing country such as South Africa, reported a slightly less female predominance at 67.2% and 32.8% of males undergoing LC in their series. The mean age reported in this series was 43 in females and 51 in males and 97% of patients had a preoperative ASA score of I/II [16].

Post operative complications and readmission has a significant burden relating to patient inconvenience, on health systems financially as well as resource utilisation

particularly on an already strained health system such as in our setting. Although the cost implication was not evaluated in this study, a meta-analysis performed by Mcintyre et,al reported a readmission rate of 3%. In the United States of America (USA), where close on 1 000 000 LC are performed annually, this would equate to 30 000 readmissions annually which is almost all index LC performed in the United Kingdom (UK) [1].

Our series delivered a surgical complication rate of 5.2% (n = 52) and an overall complication rate of 6.4% (n=64). Pucher et al, reported morbidity rates of 1.6 – 5.3% in a systematic review of complications following LC [4]. Biliary complications are the most common surgical complication [17] and there were a total of 48 biliary complications in our study. Of the 48 biliary complications, 32 patients required reintervention either with reoperation, ERCP, percutaneous drainage or a combination of the aforementioned modalities.

Biliary leak represents an unusual complication of LC. The origin of biliary leak is multifactorial, that may arise from the gallbladder bed, cystic duct, or injuries of a major bile duct. Bile leaks are reported in approximately 2% of LC [18]. There were 14 (1.4%) bile leaks recorded of which seven patients required reintervention.

BDI is a feared complication of LC and its incidence has been high since LC has become the standard compared to open cholecystectomies (OC). BDI incidence rates are reported to be 0.2-1.5% with LC and accepted to be 0.1-0.2% with OC [4,6]. BDI are commonly graded with the Strasberg Classification. Despite the completion of the learning curve and the recognition of preventive manoeuvres to avoid ductal injury during LC, the incidence rate of BDI remains unchanged [19]. This study reported a BDI rate of 0.4%.

Multiple factors are implicated in BDI and are often attributed to disease related pathology, structural misidentification and improper techniques [20,21]. The most common mechanism of such injuries involves the misidentification of the CBD or the CHD as the cystic duct or the misidentification of the hepatic artery as the cystic artery [22].

A safe cholecystectomy is one that is safe for both the patient as well as for the operating surgeon [23]. Key steps in performing a safe LC include thorough knowledge of surgically relevant anatomy, identification of factors predictive of difficult cholecystectomy, correct exposure of hepatocystic (HC) triangle in preparation of dissection, judicious use of energy sources, achieving the critical view of safety (CVS), strategies to handle a difficult situation such as stopping rules, second opinion/surgical assistance, use of intraoperative imaging to clarify the anatomy, bail-out procedure and accurate documentation [24].

There are various methods described for intraoperative assessment of biliary anatomy that may result in decreased incidence of BDI [24]. Intraoperative cholangiography (IOC) is the most commonly utilized method for the intraoperative assessment of the biliary anatomy, identification and assessment of extent of biliary injury, and possible prevention of biliary ductal injury [25].

It is a safe technique with a high success rate, and has the advantage of detection of asymptomatic CBD stones.

Many studies have demonstrated that IOC may result in lower chances of BDI and early recognition of injury. However, it does carry certain disadvantages and it’s routine use is debatable [26].

Readmissions post LC are more commonly due to surgical complications than non-surgical complications. A quality standard of less than ten percent readmission rate after cholecystectomy within the 30 day post-operative period has been recommended [27]. After any medical or surgical treatments, hospital readmission has been regarded as a measure of hospital and surgical quality of care [28,29]. Obesity, the number of coexisting diseases, conversion to open surgery, the development of intraoperative complications, the use of drain, and length of hospital stay > 1 day were significantly associated with higher readmission rates [30]. This study reported a readmission rate of 3.8%.

In a retrospective review by Rana et. al, 56% of patients were readmitted with surgical complications. In our series, 92% of patients were readmitted with surgical complications. This is significantly higher than other reported data [6]. A vast majority of the readmissions were as a result of biliary complications namely bile leak, intra-abdominal collections and retained stones.

In the US, the adoption of laparoscopic cholecystectomy has been accompanied by a 33% decrease in overall operative mortality per procedure, however cholecystectomy-related deaths has not fallen because of a 28% increase in the total rate of cholecystectomy [31].

Mortality rates in published data ranges from 0.05-0.14% [6]. This study carries a mortality of 0.3%. Although higher than most reported data, it is still similar. Mortality post LC is often related to patient confounding factors. There remains a paucity of data if mortality is directly related to surgery.

Limitations

There are some limitations that should be considered for this study. This study is retrospective in nature, although the data was extracted from a well maintained prospective database. Furthermore, a large portion of this study was conducted during the COVID-19 pandemic which resulted in a global reduction in LC as described in the CHOLECOVID study. Lastly we do not have data beyond the 30 day follow up period.

The strength of this study encompass the large population included across a surgical hospital complex which included four hospitals and a complete 30 day follow up period.

Recommendations

This data series has no follow up beyond 30 days and we recommend that an extended follow up period be evaluated. Furthermore, this study has focused on descriptive analysis of outcomes, but a more detailed analysis of the available data could be evaluated on future studies.

Conclusion

LC remains the standard of care for gallstone disease. Although it carries a higher rate of BDI, it still remains a safe procedure. The outcomes reported in our series are similar that of other published data.

References:

1. Lim SH, Salleh I, Poh BK, Tay KH. Laparoscopic cholecystectomy: an audit of our training programme. ANZ J Surg. 2005 Apr;75(4):231-3. doi: 10.1111/j.1445-2197.2005.03370.x. PMID: 15839972

2. Taki-Eldin A, Badawy AE. Outcome of laparoscopic cholecystectomy in patients with gallstone disease at a secondary level care hospital. Arq Bras Cir Dig. 2018 Jun 21;31(1):e1347. doi: 10.1590/0102-672020180001e1347. PMID: 29947681; PMCID: PMC6049991.

3. Pucher PH, Brunt LM, Davies N, Linsk A, Munshi A, Rodriguez HA, Fingerhut A, Fanelli RD, Asbun H, Aggarwal R; SAGES Safe Cholecystectomy Task Force. Outcome trends and safety measures after 30 years of laparoscopic cholecystectomy: a systematic review and pooled data analysis. Surg Endosc. 2018 May;32(5):2175-2183. doi: 10.1007/s00464-017-5974-2. Epub 2018 Mar 19. PMID: 29556977; PMCID: PMC5897463.

4. Sadler GP, Shandall A, Rees BI. Laparoscopic cholecystectomy. Br J Hosp Med. 1992 Oct 21-Nov 3;48(8):462-71. PMID: 1422557.

5. McIntyre C, Johnston A, Foley D, Lawler J, Bucholc M, Flanagan L, Sugrue M. Readmission to hospital following laparoscopic cholecystectomy: a meta-analysis. Anaesthesiol Intensive Ther. 2020;52(1):47-55. doi: 10.5114/ait.2020.92967. PMID: 32090306.

6. Rana G, Bhullar JS, Subhas G, Kolachalam RB, Mittal VK. Thirty-day readmissions after inpatient laparoscopic cholecystectomy: factors and outcomes. Am J Surg. 2016 Mar;211(3):626-30. doi: 10.1016/j.amjsurg.2015.12.007. Epub 2015 Dec 31. PMID: 26916961.

7. Rosero EB, Joshi GP. Hospital readmission after ambulatory laparoscopic cholecystectomy: incidence and predictors. J Surg Res. 2017 Nov;219:108-115. doi: 10.1016/j.jss.2017.05.071. Epub 2017 Jun 28. PMID: 29078868.

8. Mbatha SZ, Anderson F. Outcomes in laparoscopic cholecystectomy in a resource constrained environment. S Afr J Surg. 2016 Sep;54(3):8-12. PMID: 28240461.

9. Mbatha SZ, Anderson F. Outcomes in laparoscopic cholecystectomy in a resource constrained environment. S Afr J Surg. 2016 Sep;54(3):8-12. PMID: 28240461.

10. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019;95:103208. https://doi.org/10.1016/j.jbi.2019.103208.

11. Clavien PA, Barkun J, De Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The clavien-dindo classification of surgical complications: Five-year experience. Ann Surg 2009;250:187–96. https://doi.org/10.1097/SLA.0b013e3181b13ca2.

12. KarimianF,AminianA,MirsharifiR,MehrkhaniF:Surgical options in the management of cystic duct avulsion during laparoscopic cholecystectomy. Patient Safety in Surgery 2008; 2:17.

13. Passos MA, Portari-Filho PE. Antibiotic prophylaxis in laparoscopic cholecistectomy:is it worth doing?ArqBrasCirDig.2016Jul-Sep;29(3):170-172.

14. Nuzzo G, Giuliante F, Giovannini I, Ardito F, D'Acapito F, Vellone M, et al: Bile duct injuryduring laparoscopic cholecystectomy: results of an Italian national survey on cholecystectomies. Arch Surg 2005;140:986–992.

15. Khan, Z.A., Khan, M.U. & Brand, M. Increases in cholecystectomy for gallstone related disease in South Africa. *Sci Rep* 10, 13516 (2020). https://doi.org/10.1038/s41598-020-69812-3

16. Coelho JCU, Dalledone GO, Schiel W, Berbardin JP, Claus CMP, Marias JEF, Freitas ACT. Does male gender increase the risk of laparoscopic cholecystectomy? ABCD Arq Bras Cir Dig. 2019;32(2):e1438. DOI: /10.1590/0102-672020190001e1438

17. Agabiti N, Stafoggia M, Davoli M*, et al.* Thirty-day complications after laparoscopic or open cholecystectomy: a population-based cohort study in Italy. *BMJ Open* 2013;**3:**e001943. doi: 10.1136/bmjopen-2012-001943

18. Fouad MMB, Rezk SSS, Saber AT, Khalifa A, Ibraheim P, Ibraheim SMN. Effect of the COVID-19 Pandemic on the Management of Acute Cholecystitis and Assessment of the Crisis Approach: A Multicenter Experience in Egypt. Asian J Endosc Surg. 2022 Jan;15(1):128-136. doi: 10.1111/ases.12980. Epub 2021 Sep 1. PMID: 34468089; PMCID: PMC8652686.

19. Chun K. Recent classifications of the common bile duct injury. Korean J Hepatobiliary Pancreat Surg. 2014 Aug;18(3):69-72. doi: 10.14701/kjhbps.2014.18.3.69. Epub 2014 Aug 31. PMID: 26155253; PMCID: PMC4492327.

20. Strasberg SM, Hertl M, Soper NJ. An analysis of the problem of biliary injury during laparoscopic cholecystectomy. *J Am Coll Surg* 1995; 180: 101-125 [PMID: 8000648 DOI: 10.1006/jsre.1995.1018]

21. Callery MP. Avoiding biliary injury during laparoscopic cholecystectomy: technical considerations. *Surg Endosc* 2006; 20: 1654-1658 [PMID: 17063288 DOI: 10.1007/s00464-006-0488-3]

22. Iwashita Y, Hibi T, Ohyama T, Umezawa A, Takada T, Strasberg SM, Asbun HJ, Pitt HA, Han HS, Hwang TL, Suzuki K, Yoon YS, Choi IS, Yoon DS, Huang WS, Yoshida M, Wakabayashi G, Miura F, Okamoto K, Endo I, de Santibañes E, Giménez ME, Windsor JA, Garden OJ, Gouma DJ, Cherqui D, Belli G, Dervenis C, Deziel DJ, Jonas E, Jagannath P, Supe AN, Singh H, Liau KH, Chen XP, Chan ACW, Lau WY, Fan ST, Chen MF, Kim MH, Honda G, Sugioka A, Asai K, Wada K, Mori Y, Higuchi R, Misawa T, Watanabe M, Matsumura N, Rikiyama T, Sata N, Kano

N, Tokumura H, Kimura T, Kitano S, Inomata M, Hirata K, Sumiyama Y, Inui K, Yamamoto M. Delphi consensus on bile duct injuries during laparoscopic cholecystectomy: an evolutionary cul-de-sac or the birth pangs of a new technical framework? *J Hepatobiliary Pancreat Sci* 2017; 24: 591-602 [PMID: 28884962 DOI: 10.1002/jhbp.503]

23. Gupta V. ABCD of Safe Laparoscopic Cholecystectomy: Imbibing Universal Culture of Safety in Cholecystectomy. *Indian J Surg* 2018 [DOI: 10.1007/s12262-018-1775-7]

24. Gupta V, Jain G. Safe laparoscopic cholecystectomy: Adoption of universal culture of safety in cholecystectomy. World J Gastrointest Surg. 2019 Feb 27;11(2):62-84. doi: 10.4240/wjgs.v11.i2.62. PMID: 30842813; PMCID: PMC6397793.

25. Alvarez FA, de Santibañes M, Palavecino M, Sánchez Clariá R, Mazza O, Arbues G, de Santibañes E, Pekolj J. Impact of routine intraoperative cholangiography during laparoscopic cholecystectomy on bile duct injury. *Br J Surg* 2014; 101: 677-684 [PMID: 24664658 DOI: 10.1002/bjs.9486]

26. Eikermann M, Siegel R, Broeders I, Dziri C, Fingerhut A, Gutt C, Jaschinski T, Nassar A, Paganini AM, Pieper D, Targarona E, Schrewe M, Shamiyeh A, Strik M, Neugebauer EA; European Association for Endoscopic Surgery. Prevention and treatment of bile duct injuries during laparoscopic cholecystectomy: the clinical practice guidelines of the European Association for Endoscopic Surgery (EAES). *Surg Endosc* 2012; 26: 3003-3039 [PMID: 23052493 DOI: 10.1007/s00464-012-2511-1]

27. Awolaran O, Gana T, Samuel N, Oaikhinan K. Readmissions after laparoscopic cholecystectomy in a UK District General Hospital. Surg Endosc. 2017;31:3534-8.

28. Fragua RL, Vázquez AM, Pérez CR, Velasco AA, Marcano AL, Peralta A, et al. Readmission rates after laparoscopic cholecystectomy:are they affected by ERCP prior to surgery?Rev Esp Enferm Dig. 2019;111:460-6.

29. Manuel-Vázquez A, Latorre-Fragua R, Ramiro-Pérez C, Lopez-Marcano A, Al-Shwely F, Plaza-Llamas R, et al. Ninety-day readmissions after inpatient cholecystectomy:a 5-year analysis. World J Gastroenterol. 2017;23:2972-7 (25)

30. Hacim NA, Akbas A, Gullu HF, Ulgen Y, Karabay O, Meric S, Aktokmakyan TV, Altinel Y. 90-day readmission rates after cholecystectomy: A retrospective cohort study. Cir Cir. 2022;90(S1):70-76. English. doi: 10.24875/CIRU.21000371. PMID: 35944101.

31. Steiner CA, Bass EB, Talamini MA, Pitt HA, and Steinberg EP. Surgical Rates and Operative Mortality for Open and Laparoscopic Cholecystectomy in Maryland. N Engl J Med 1994; 330:403-408. DOI: 10.1056/NEJM199402103300607

Part B: Supporting Documents

Addendum A: Abbreviations pg. 33

Addendum B: Index of tables pg. 34

Addendum C: Author Guidelines of World Journal of Surgery pg. 35

Addendum D: Departmental Research Committee approval pg. 38

Addendum E: HREC approval pg. 39

Addendum A: Abbreviations

ASA	–	American Society of Anaesthesiologist
BDI	–	Bile Duct Injury
BMI	–	Body Mass Index
CBD	–	Common Bile Duct
ECCR	–	Electronic Continuity of Care Record
ERCP	–	Endoscopic Retrograde Cholangiopancreatogram
ICU	–	Intensive Care Unit
LC	–	Laparoscopic Cholecystectomy
LSC	–	Laparoscopic Subtotal Cholecystectomy
NHLS	–	National Health Laboratory Service
OC	–	Open Cholecystectomy
PACS	–	Picture Archiving and Communication System
REDCap	–	Research Electronic Data Capture
UCT	–	University of Cape Town
UK	–	United Kingdom
USA	–	United States of America

Addendum B: Index of Tables

Table 1: Demographic characteristics of patients undergoing laparoscopic cholecystectomy in the Cape Metro West Region from September 1, 2019 through July 31 2022.

Table 2: Indications for patients undergoing laparoscopic Cholecystectomy according to gender and admission type from September 1 2019 through July 31 2022

Table 3: Surgical and non-surgical complications from patients undergoing laparoscopic cholecystectomy in the Cape Metro West from September 1 2019 through July 31 2022

Table 4: Calvien-dindo grading per complication for patients undergoing Laparoscopic Cholecystectomy from September 1 2019 through July 31 2022

Table 5: Readmissions for patients undergoing Laparoscopic Cholecystectomy from September 1 2019 through July 31 2022

Table 6: Clavien-Dindo grading for readmissions per complication for patients undergoing Laparoscopic Cholecystectomy from September 1 2019 through July 31 2022

Addendum C: Author guidelines of World Journal of Surgery

MANUSCRIPT PREPARATION AND ORGANIZATION

General instructions:
• Use a normal, plain font (e.g., 10-12 point Times Roman or Arial) for text • Double-space the text
• Use italics for emphasis
• Include page numbers
• Do not use field functions
• Use tab stops or other commands for indents, not the space bar
• Use the table function, not spreadsheets, to make tables

Manuscript style and text formatting:

Styling and text formatting refers to the use of special effects to enhance the appearance of the published article. Please make note of the following "Dos and Don'ts" regarding styling:
• DO enter all lists as single column lists.
• DO use your word processing features to indicate bold, italic, superscript, and subscript text within a paragraph or heading.

• DO NOT center text for headings. All text should be justified left, with ragged (unjustified) right margins.
• DO NOT use italic, underline, or other type effects for the entire text of a heading.
• DO NOT use all capital letters for a heading; use initial caps instead.

• DO NOT use multiple spaces to set up columns or tables; use tabs instead.
• DO NOT use carriage returns at the end of each line of text (use the word wrap feature).

Manuscript organization:

Manuscripts should be organized and follow the sequence as indicated below:
TITLE PAGE: The title page should include:
• A concise and informative title
• The name(s) of the author(s) including the affiliation(s) and address(es) of each author. The complete name and address of the author to whom correspondence should be sent, as well as his/her phone number, fax number, and email address.

• A short title for use as a running head
• Keywords: 3-6 keywords relevant to the manuscript

• Trail registration number for randomized clinical trials (see “Types of Manuscripts: Original Scientific Reports” above)
• Grant support for the research reported
• Statements to comply with ethical requirements (see “Compliance with Ethical Requirements” below for more details):

- ¨ A statement for each author in the manuscript must be included declaring whether there are any conflicts of interest in the manuscript. Even if there is no conflict of interest, this should also be explicitly stated as none declared on the title page.
- ¨ Statement of informed consent should be included if individual participants are included in the study. For example: “Informed consent was obtained from all individual participants included in the study.”
- ¨ Statement of human and/or animal rights should be included (if applicable) stating that the study was approved by the appropriate institution and/or national research ethics committee

Manuscript word count of your submission

ABSTRACT (if applicable):
The abstract must appear between the title page and the Introduction section of the manuscript, even if it has been uploaded separately. Manuscripts that require an abstract should contain a structured abstract of not more than 250 words. It should be a factual description of the study performed organized with the headings of: *Background* (includes aims, hypotheses, or objectives), *Methods* (includes patient population, procedures, and data analysis), *Results*, and *Conclusions.*

The abstract should contain the data to support the key findings or conclusions of the study. The trial registration number for randomized clinical trials must be included at the end of the abstract. The first time an abbreviated term is used, spell it out in full and follow with the abbreviation in parentheses – for example: ultrasound (US).

TEXT:

Original Scientific Reports should be arranged in sections titled Introduction, Material and Methods, Results, and Discussion.
1. Introduction: conveys the background and purpose of the report
2. Material and Methods

3. Results & Discussion
When required by the nature of the report, manuscripts that do not follow this specific format may be accepted.

ACKNOWLEDGEMENTS:

A brief statement should acknowledge individuals, other than authors, who were of direct help in the reported work or if the work was supported by a federal or commercial grant. All acknowledged persons should give their written consent to being named in the manuscript. This consent is to be uploaded upon manuscript submission.

REFERENCES:

Reference citations in the text should be identified by numbers in brackets (e.g. [4]). Number the references in order of their first appearance in the text (not alphabetically). Once a reference is cited, all subsequent citations should be to the

original number. References may not appear in your Reference List unless they have been cited in the text or tables. Manuscripts that have been accepted for publication or are in press may be listed as references, but the Journal does not reference unpublished data and personal communications. Use the form for references adopted by the U.S. National Library of Medicine, as in Index Medicus. For each reference, show inclusive page ranges (e.g., 7-19).

UNIVERSITY OF CAPE TOWN

Department of Surgery
Departmental Research Committee
A/Prof Maritz Laubscher
Groote Schuur Hospital
Observatory 7925
South Africa
Tel (021) 404 5108
Email: **maritz.laubscher@uct.ac.za**

18 Jun 2021

Dr M Kariem

Department of Surgery
University of Cape Town

Dear Dr Kariem

RE: Project 2021/214

PROJECT TITLE: 30 Day Outcomes Of 1000 Consecutive Laparoscopic Cholecystectomies Across Four Metropole Hospitals In Cape Town

The above protocol has been reviewed by the Department of Surgery Research Committee. I am pleased to inform you that the committee approved the scientific merit of the study, and endorse the protocol for submission to the relevant ethics committee.

Although this letter serves as confirmation that the above protocol has successfully passed through the surgical DRC, respective ethics committees still require DRC chair signature before submission.

Please use the above project number in all future correspondence,

Yours sincerely

A/PROF MARITZ LAUBSCHER
CHAIR SURGICAL DRC

"OUR MISSION is to be an outstanding teaching and research university, educating for life and addressing the challenges facing our society."

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

12 July 2021

HREC REF: 430/2021

Dr J Kloppers
Department of General Surgery
F-25, NGSH
Email: christo.kloppers@uct.ac.za
Student: macateen@gmail.com

Dear Dr Kloppers

PROJECT TITLE: 30 DAY OUTCOMES OF 1000 CONSECUTIVE LAPAROSCOPIC CHOLECYSTECTOMIES ACROSS FOUR METROPOLE HOSPITALS IN CAPE TOWN-MMED CANDIDATE-DR MAAHIR KARIEM-SUB-STUDY LINKED TO R040/2019

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 & 06 July 2020.

Approval is granted for one year until the 30 July 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Maahir Kariem will also be involved in this study.

Please quote the HREC REF 430/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

HREC/REF430/2021sa

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) **This serves as notification of annual approval, including any documentation described below.**			
☑ Approved	Annual progress report	Approved until/next renewal date	30.8.2024
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee	[signature]	Date Signed	7/8/2023

Note: Please email this form and supporting documents (if applicable) in a combined PDF to hrec-enquiries@uct.ac.za.
Please clarify your plan for research-related activities during COVID-19 lockdown.
Please use the latest form found on our website:
http://www.health.uct.ac.za/fhs/research/humanethics/forms

HUMAN RESEARCH ETHICS COMMITTEE
- 7 AUG 2023
HEALTH SCIENCES FACULTY UNIVERSITY OF CAPE TOWN

Comments to PI from the HREC
Thank you for your Study Deviation HREC Chair Signature [signature] Date: 7/8/2023

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	01/08/2023		
HREC REF Number	430/2021	Current Ethics Approval was granted until	30/07/2022
Protocol title	30 day outcomes of 1000 consecutive laparoscopic cholecystectomies across four Metropole Hospitals in Cape Town		
Protocol number (if applicable)	2021/214		
Are there any sub-studies linked to this study?	☐ Yes	☑ No	
If yes, could you please provide the HREC Reference number for all sub-studies? **Note:** A separate FHS016 must be submitted for each sub-study.			
Principal Investigator	Professor Christo Kloppers		

28 February 2022 Page 1 of 7 FHS016

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)