Surgery in Practice and Science 15 (2023) 100219

Contents lists available at ScienceDirect

Surgery in Practice and Science

journal homepage: www.sciencedirect.com/journal/surgery-in-practice-and-science

Outcomes in COVID-19 patients undergoing laparoscopic cholecystectomy/appendectomy in the pre-vaccine era

Steven K.M. Vuu [a,c,*], Huazhi Liu [c], Darwin N. Ang [a,b,c]

[a] *University of Central Florida College of Medicine, United States*
[b] *University of South Florida Morsani College of Medicine, United States*
[c] *Ocala Regional Medical Center, Ocala, FL, United States*

ARTICLE INFO

Keywords:
COVID-19
Cholecystectomy
Appendectomy

ABSTRACT

Background: We hypothesized that COVID-19 positive patients requiring laparoscopic cholecystectomy (lap chole) or appendectomy (lap appy) would have increased inpatient mortality rates compared to all COVID-19 patients.
Methods: Retrospective cohort analysis including COVID-19 patients from 1/1/20 to 9/30/20. 82,574 cases identified. Patients excluded if <18 years old or underwent surgery other than lap chole or lap appy. Control groups were patients without surgery ($N = 82{,}145$). Exposure groups underwent lap chole ($N = 323$) or lap appy ($N = 106$). Primary outcome was inpatient mortality. Secondary outcomes included hospital length of stay (LOS) and complications such as bacterial pneumonia, deep venous thrombosis (DVT), pulmonary embolism (PE), urinary tract infection (UTI), acute myocardial infarction (MI), acute respiratory distress syndrome (ARDS), and respiratory failure (RF).
Results: Overall inpatient mortality rate was 32.8% in COVID-19 patients undergoing lap chole (p-value <0.0001), 2.8 % lap appy (p-value 0.93), and 1.2 % in control group. ARDS complication rate was 11.2 % in lap chole (p-value <0.0001), 1.9 % lap appy (p-value 0.71), and 0.2 % in control.
Conclusion: COVID-19 patients during the initial wave of the pandemic who underwent lap chole during hospital admission had significantly higher risk of mortality and ARDS while lap appy did not.

Introduction

Several studies have published data that show higher postoperative mortality and complications in COVID-19 patients [1,2,12-15]. The COVID Surg Collaborative, an international collaborative of surgeons spanning 122 countries, conducted an international, multi-center, cohort study at 235 hospitals in 24 countries including 1128 patients, and found that "postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 (COVID-19) infection and are associated with high mortality" [1]. Due to these increased risks, their recommendations included a higher threshold for surgery. The decision whether to proceed with surgery in COVID-19 patients or recommend non-operative management has proven to be challenging for surgeons and their teams [12,13]. Most studies have looked at outcomes in patients undergoing unspecified abdominal surgery [14,15] but there has been limited data specifically on two common laparoscopic general surgery procedures, namely, laparoscopic appendectomy (lap appy) and laparoscopic cholecystectomy (lap chole).

Our study aims to examine the clinical outcomes of patients with COVID-19 who underwent lap appy or lap chole during the pre-vaccine era. This would provide insight into patient outcomes who were COVID-19 positive who underwent surgery or no surgery before vaccination. There was also data that showed that unvaccinated people were 13 times more likely to become infected and 20 times more likely to die than fully vaccinated people [2]. We believe that this would be valuable in providing education towards informing patients who are unvaccinated and COVID-19 positive considering urgent surgery. We hypothesized that COVID-19 positive patients admitted to the hospital requiring lap chole or lap appy would have increased inpatient mortality rates compared to all COVID-19 patients.

* Corresponding author.
E-mail address: steven.vuu@ucf.edu (S.K.M. Vuu).

https://doi.org/10.1016/j.sipas.2023.100219

Available online 16 September 2023

Methods

Study design and population

A retrospective cohort study of a clinical database within a large hospital system in the United States was performed, selecting for patients diagnosed with COVID-19 from January 1, 2020 to September 30, 2020. All participating hospitals are a part of a single health care system and use the same electronic medical record (EMR) software. The data were entered into a centralized dataset in a secured server within the hospital system's clinical data warehouse and subsequently abstracted as de-identified data. A formal Institutional Review Board (IRB) process deemed this study as exempt.

There were a total of 93,918 patients with confirmed cases of COVID-19 within the period of study. Patients were excluded if they were less than 18 years old or underwent any surgery other than lap chole or lap appy. After excluding 11,344 patients, a total of 82,574 cases were included in our study. Laboratory confirmation of COVID-19 infection was performed using the following tests: A SARS Antigen Fluorescent Immunoassay (FIA) was utilized for qualitative detection of the nucleocapsid protein from SARS-CoV-2. Direct nasal swabs were used as samples. Positive samples were confirmed using a nucleic acid amplification protocol. Positive samples were confirmed using direct real-time RT-PCR assay. Only laboratory-confirmed cases were included in this analysis. None of the patients in our study were vaccinated as this is a period of time before vaccination.

Study cohorts, variables, and outcomes

The control group were patients who did not undergo surgery while the exposure group did undergo surgery. The non-operative group included 82,145 COVID-19 positive patients. The operative group included 323 COVID-19 positive patients who underwent lap chole and 106 COVID-19 positive patients who underwent lap appy (Fig. 1). The control group (non-operative treatment) was further subdivided into patients with biliary disease who did not undergo surgery (symptomatic cholelithiasis and acute cholecystitis). The exposure groups (operative treatment) were subdivided similarly (symptomatic cholelithiasis and acute cholecystitis) and the two different treatment groups were compared for differences in mortality rate. To examine the baseline mortality rate, we also examined the cohort of patients who had lap chole or lap appy who did not have COVID-19 during the same period of time. Demographic information collected included age, gender, race, insurance status, and comorbidities (Table 1). Comorbidities and secondary outcomes were captured using ICD-10 codes as follows: Coronary artery disease (CAD) I25.10, congestive heart failure (CHF) I50, malignant neoplasm C80.1, chronic obstructive pulmonary disease (COPD) J44.9, asthma J45, history of stroke I63.9, Alzheimer Disease G30.9, diabetes E11.9, chronic kidney disease (CKD) N18.9, cannabis use F12.90, alcohol abuse F10.1, obesity (body mass index >30) E66.9, and tobacco smoker F17.200. The primary outcome of the study was inpatient mortality (Table 3). Secondary outcomes included postoperative complications such as bacterial pneumonia (PNA) J18.9, deep venous thrombosis (DVT) I82.40, pulmonary embolism (PE) I26.9, urinary tract infection (UTI) N39.0, acute myocardial infarction (MI) I21.XX, Acute Respiratory Distress Syndrome (ARDS) J80, respiratory failure (RF) J96.XX, bile leak (K83.2), intra-abdominal abscess (K65.1, T81.43X), surgical site infection (T81.41X, T81.42X), hospital disposition, and hospital length of stay (LOS) (Tables 2 and 3).

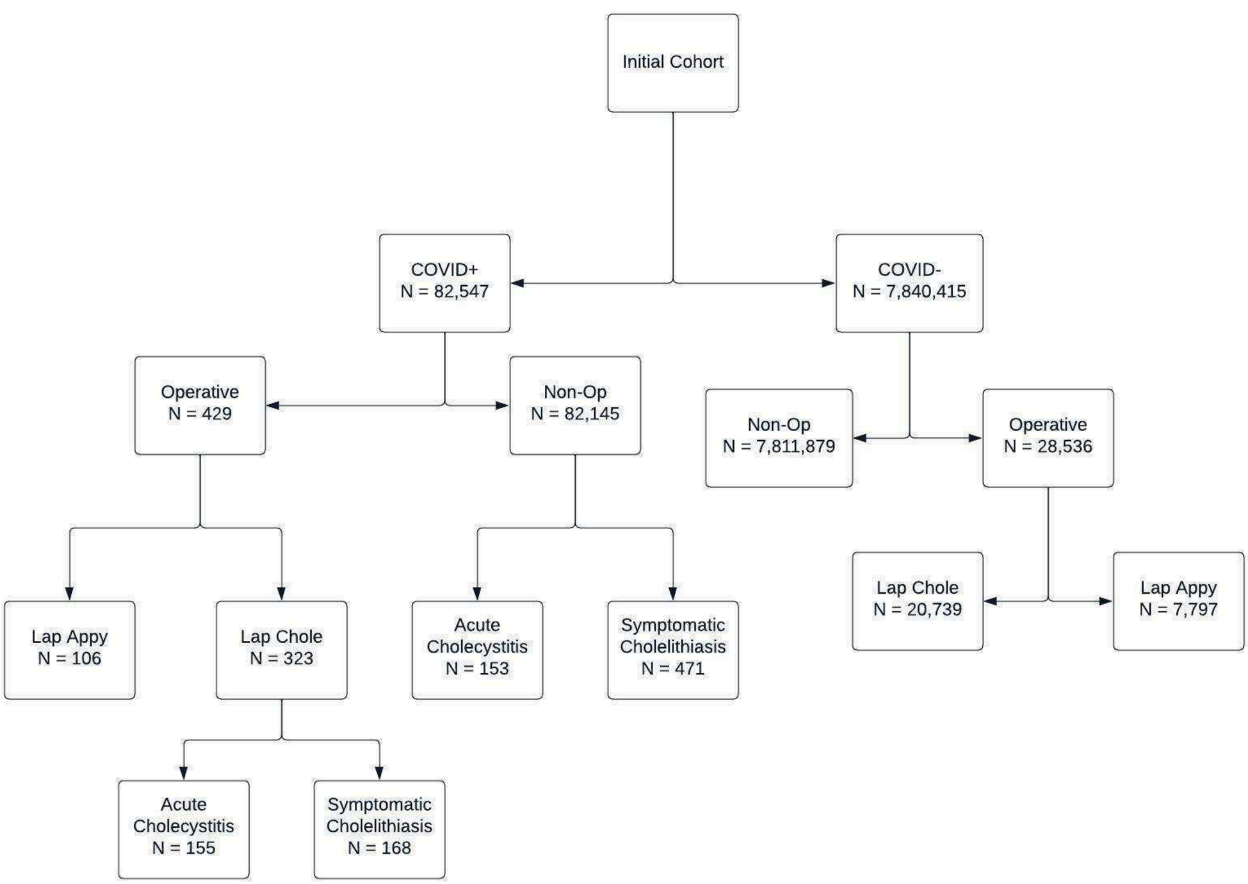

Fig. 1. Study Population.

Table 1
Patient Demographics.

	COVID-19 without Surgery $N =$ 82,145	COVID-19 with Lap Chole $N =$ 323	COVID-19 with Lap Appy $N =$ 106	p-values
Age				
18–44	39.7%	18.3%	67.9%	<0.0001
45–54	16.5%	14.6%	13.2%	0.43
55–64	15.8%	15.8%	8.5%	0.12
65–74	12.9%	26.0%	4.7%	<0.0001
75–84	9.4%	17.3%	4.7%	<0.0001
>=85	5.7%	8.1%	0.9%	0.02
age (mean)	51.5 (±19.6)	61.8 (±17.4)	39.2 (±17.5)	<0.0001
age (median)	51	65	35	
age (mode)	90	79	19	
Gender				
Male	46.7%	53.2%	60.4%	0.001
Female	53.3%	46.8%	39.6%	0.001
Race				
White	48.3%	53.9%	61.3%	0.004
Black	24.0%	17.3%	4.7%	<0.0001
Asian	2.0%	2.5%	0.9%	0.61
Other	23.3%	24.8%	27.4%	0.50
Unknown	2.4%	1.6%	5.7%	0.06
Insurance				
Blue Cross/Cost	3.0%	2.5%	2.8%	0.84
Commercial	20.1%	13.9%	24.5%	0.01
Government	23.5%	8.7%	10.4%	<0.0001
Medicaid	13.2%	13.6%	11.3%	0.83
Medicare	29.7%	50.2%	13.2%	<0.0001
Other	7.6%	8.7%	25.5%	<0.0001
Self-Pay	1.7%	1.6%	11.3%	<0.0001
Worker's Comp.	1.1%	0.9%	0.9%	0.92
Comorbidities				
Coronary artery disease I25.10 (CAD)	8.6%	22.3%	8.5%	<0.0001
CHF (I50)	7.1%	30.0%	4.7%	<0.0001
Malignant neoplasm C80.1?	0.02%	0.0%	0.0%	0.96
COPD J44.9	2.2%	3.7%	0.9%	0.12
Asthma J45	6.9%	6.8%	7.6%	0.96
History of stroke I63.9	0.3%	0.9%	1.9%	0.001
Alzheimer's Disease G30.9	1.1%	1.9%	0.0%	0.23
Diabetes E11.9	12.8%	12.7%	4.7%	0.05
CKD N18.9	2.3%	10.3%	0.0%	<0.0001
Cannabis use F12.90	0.4%	1.2%	2.8%	<0.0001
Alcohol abuse F10.1	0.7%	2.5%	1.9%	0.0002
Obesity (BMI >30) E66.9	8.2%	20.4%	18.9%	<0.0001
Tobacco Smoker F17.200	6.3%	6.5%	12.3%	0.04

Statistical analysis

Continuous data were expressed as mean with standard deviation (SD). Parametric data expressed as proportions were evaluated by Chi-square tests and Student *t-tests* for continuous variables. Non-parametric data were evaluated by Fisher's exact test for proportions and the Wilcoxon-Rank-Sum test for continuous variables. Multivariable regression was performed to adjust for age, gender, race, BMI >30, Charlson Comorbidity Index, and tobacco smoking status. Logistic regression was used for binary outcomes and linear regression methods were used for continuous outcomes. All statistical analyses were performed using SAS 9.4. P-values were statistically significant if <0.05.

Results

Tables 1 to 3 provides descriptive analyses amongst the 3 cohorts.

Table 2
Hospital Disposition.

Hospital Disposition	COVID-19 without Surgery $N =$ 82,145	COVID-19 with Lap Chole $N =$ 323	COVID-19 with Lap Appy $N =$ 106
home or self care (routine discharge)	79.6%	29.1% <0.0001	84.9% 0.18
home under care	4.1%	6.8% 0.02	2.8% 0.50
Inpatient Rehab Facility (IRF)	0.6%	5.0% <0.0001	0.0% 0.41
long term care hospital (ltch)	0.4%	6.2% <0.0001	3.8% <0.0001
short term general hospital	2.6%	1.6% 0.24	1.9% 0.65
Skilled Nursing Facility (SNF)	6.6%	6.8% 0.86	1.9% 0.05
Expired	1.2%	32.8% <0.0001	2.8% 0.14
Hospice	1.9%	10.5% <0.0001	0.0% 0.15
Others	2.9%	1.2% 0.08	1.9% 0.54

Multivariable regression was performed to adjust for age, gender, race, obesity, Charlson comorbidity index, and tobacco smoking status. In terms of socio-demographics, the median age was 51 in the control group, 65 in the lap chole group, and 35 in the lap appy group. The majority of lap appy patients (67.9%) were between ages 18–44. The largest proportion of lap chole patients were in the age 65–74 bracket (26.0%). The largest proportion of the control group were in the age 18–44 bracket (39.7%). The majority of the control group was female (53.3%). The lap chole group was 53.2% male while the lap appy group was 60.4% male. Overall race was similar amongst the 3 cohorts, with the exception of 24.0% of the control group being Black, a higher rate compared to the lap chole and lap appy groups at 17.3% and 4.7% respectively. In terms of hospital disposition, the lapcholecohort had significantly higher rates of discharge to inpatient rehab 5%, home under care (6.8%), LTCH (6.2%), and hospice (10.5%_. The lapappy-cohort had higher rates of discharge to LTCH (3.8%). With respect to comorbidities, the lap chole group had a higher percentage of patients with CAD (22.3%), CKD (10.3%), CHF (30.0%), and alcohol abuse (2.5%). The control group had the highest rates of asthma (6.9%) and diabetes (12.8%) compared to the exposure groups. Obesity rates were 8.2% in the control group, 20.4% in the lap chole group, and 18.9% in the lap appy group. Multivariable regression analysis was performed to account for these differences.

Table 3 provides data on the outcomes and complications. Multivariable regression was performed to adjust for age, gender, race, obesity, Charlson Comorbidity Index, and tobacco smoking status. The control group had an inpatient mortality rate of 1.2%. The lap chole group had the highest inpatient mortality rate at 32.8% (adjusted p-value of <0.0001). The lap appy group also had a mortality rate of 2.8% (adjusted p-value of 0.93). In terms of secondary outcomes, ARDS was highest in the lap chole group at 11.2% with an adjusted p-value of <0.0001 compared to the control group at 0.2%. 1.9% of patients in the lap appy group developed ARDS which was not statistically significant compared to the control group. 63.2% of lap chole patients developed respiratory failure after surgery compared to 22.0% in the control group with an adjusted p-value of <0.0001. There were also higher rates of UTI in the lap chole group (14.9%) compared to the control group (5.8%), adjusted p-value 0.02. Finally, there were no significant differences in secondary outcomes amongst the 3 cohorts with respect to bacterial pneumonia, DVT, PE, surgical site infection, abscess, bile leak, or MI.

In order to investigate the high mortality rate in cholecystectomy patients in this study cohort, we performed a subset analysis in table 4 comparing COVID-19 negative patients who did not undergo surgery to

Table 3
Primary and Secondary Outcomes.

	COVID-19 without Surgery $N = 82{,}145$	COVID-19 with Lap Chole $N = 323$	COVID-19 with Lap Appy $N = 106$
Inpatient Mortality	1.2%	32.8%	2.8%
p-value		<0.0001	0.09
adjusted p-value		<0.0001 *	0.98 *
Hospital LOS	3.1 (±5.6)	18.9 (±18.0)	6.5 (±15.7)
p-value		<0.0001	<0.0001
adjusted p-value		<0.0001 *	<0.0001 *
Complications			
Bacterial Pneumonia	3.2%	2.5%	1.9%
p-value		0.99	0.58
adjusted p-value		0.84 *	0.73 *
Deep Venous Thrombosis (DVT)	0.2%	1.9%	0.0%
p-value		0.97	0.97
adjusted p-value		0.97 *	0.98 *
Pulmonary embolism (PE)	0.8%	3.1%	0.9%
p-value		0.03	0.60
adjusted p-value		0.24 *	0.93 *
Urinary Tract Infection (UTI)	5.8%	14.9%	3.8%
p-value		<0.0001	0.06
adjusted p-value		0.02 *	0.64 *
Acute myocardial infarction (MI)	1.8%	9.9%	0.0%
p-value		0.91	0.93
adjusted p-value		0.93 *	0.94 *
Acute respiratory distress syndrome (ARDS)	0.2%	11.2%	1.9%
p-value		<0.0001	0.90
adjusted p-value		<0.0001 *	0.68 *
Respiratory failure (RF)	22.0%	63.2%	12.3%
p-value		<0.0001	<0.0001
adjusted p-value		<0.0001 *	<0.0001 *
Bile Leak	0.0001%	0.0%	0.0%
p-value		0.99	0.99
adjusted p-value		0.99*	0.99*
Abscess	0.03%	1.2%	0.0%
p-value		0.98	0.99
adjusted p-value		0.97*	0.98*
Surgical Site Infection	0.05%	0.0%	0.9%
p-value		0.99	0.98
adjusted p-value		0.95*	0.94*

* Adjusted by age, race, gender, obesity (BMI>30), Charlson Comorbidity Index, tobacco smoker.

Table 4
Mortality rates of appendectomy and cholecystectomy patients based on COVID status during the same time period.

	COVID-19 without Surgery ($N = 82{,}145$)	COVID-19 with Lap Chole ($N = 323$)	COVID-19 with Lap Appy ($N = 106$)
Inpatient Mortality	1.20%	32.80%	2.80%
	NO COVID-19 without Surgery ($N = 7811{,}879$)	NO COVID-19 with Lap Chole ($N = 20{,}739$)	NO COVID-19 with Lap Appy (**$N = 7797$**)
Inpatient Mortality	0.50%	1.40%	0.30%

COVID-19 negative patients who underwent lap chole or lap appy as a baseline comparison. There was a 0.5% mortality rate in COVID-19 negative, non-surgical patients ($N = 7811{,}879$), a 1.4% mortality rate in COVID-19 negative patients who underwent lap chole ($N = 20{,}739$), and a 0.3% mortality rate in COVID-19 negative patients who underwent lap appy ($N = 7797$). Finally, we compared the mortality rates in COVID-19 patients with symptomatic cholelithiasis and acute cholecystitis who underwent surgical versus non surgical treatment. We found a 2.8% mortality rate in COVID-19 positive, symptomatic cholelithiasis patients who did not undergo surgery compared to 42.3% who underwent lap chole (p-value <0.0001) and a 1.3% mortality rate in COVID-19 positive, acute cholecystitis patients who did not undergo surgery compared to 22.6% who underwent lap chole (p-value <0.0001).

Discussion

The decision of whether or not to operate on COVID-19 patients are influenced by many factors, including the risks and benefits of definitive treatment and the potential concern for increased risk of exposure to the surgical team. To date, there has been no evidence of aerosolization of COVID-19 viral particulate matter during laparoscopic surgery or in surgical smoke [3,5–7]. However, there has been data that COVID-19 has been detected in peritoneal fluid[8]. It is important to minimize risk of exposure by keeping insufflation pressures low, minimizing the length of laparoscopic incisions to reduce leakage, and careful desufflation of the abdomen at the end of the case [4].

According to the Tokyo Guidelines, the accepted mortality rate of acute cholecystitis should be less than 1% [9]. During the pandemic era, the American College of Surgeons published guidelines regarding the management of biliary colic and acute cholecystitis. Their recommendations were to proceed with surgery in cases of mild acute cholecystitis (WBC <18 K, <72 h time from onset, no evidence of abscess, gangrene, or systemic organ failure) if resources are ample, and non operative management with antibiotics, dietary modifications, and subsequent interval cholecystectomy at 3 months if resources are limited. Percutaneous cholecystostomy was reserved for refractory cases. In mild acute cholecystitis, the operation is often less challenging, resulting in decreased operative time and complications. They recommended non operative treatment for moderate acute cholecystitis (WBC >18 K, >72 h time from onset, evidence of abscess, gangrene, without systemic organ failure) and severe acute cholecystitis (requiring ICU care, signs of systemic organ failure) [10].

The lap chole cohort of 323 COVID-19 patients had an overall inpatient mortality rate of 32.8% (adjusted p-value of <0.0001), which is a 32 fold increase in mortality risk compared to COVID-19 positive patients without surgery (Table 3). To compare similar groups, we substratified COVID-19 positive patients with biliary disease by treatment status (operative vs nonoperative) and type of biliary disease (symptomatic cholelithiasis and acute cholecystitis). We found similar results with high mortality in the operative group for symptomatic cholelithiasis (42.3% vs. 2.8%, adjusted p-value <0.0001) and for acute cholecystitis (22.6% vs. 1.3%, adjusted p-value <0.0001) (Table 5). The higher rate of mortality in symptomatic cholelithiasis is unclear; however, patients who had symptomatic cholelithiasis may have been admitted to the hospital for other vague symptoms related to COVID-19 whereas patients who had acute cholecystitis were likely to present with true acute biliary disease. The lapcholecohort did have a higher incidence of CAD, CHF, and CKD, which may have had an association with higher mortality and ARDS observed, however, these comorbidities

Table 5
Mortality of COVID positive patients based on treatment (operative vs. nonoperative) for symptomatic and acute cholecystitis.

	Mortality (Nonoperative) $N =$	Mortality (Operative)	Adjusted p-value
COVID+ Symptomatic Cholelithiasis	2.8% $N = 471$	42.3% $N = 168$	<0.0001
COVID+ Acute Cholecystitis	1.3% $N = 153$	22.6% $N = 155$	<0.0001

were adjusted with multivariable regression to account for these differences. Another potential limitation to this study is that we did not have the data for the mean or median duration of surgery and wonder whether this would have contributed to the differences in outcomes. Regardless, these mortality rates are beyond those set by Tokyo Guidelines and high by any other standards. In addition, hospital length of stay was also protracted with a mean of 18.9 days (adjusted p-value <0.0001). The high mortality rates were associated with higher postoperative complications such as a 2.8 fold increased risk of respiratory failure and a 56 fold increased risk of ARDS and may explain the ultimate mechanism of death.

Because of such high mortality rates in the lap chole group, we compared these outcomes with COVID-19 negative patients who underwent lap chole as a baseline and found only a 1.4% mortality rate suggesting that the increased mortality was due to the combination of COVID-19 status and undergoing surgery. Additionally, while this study focuses on a specific hospital system, we cannot make direct comparisons to other systems without further data, especially median age differences amongst different hospital groups which may contribute to differing mortality rates.

Due to the high mortality risk of this patient population, especially in the unvaccinated who remain a significant proportion of the population. Our findings may help add to a meaningful discussion with the patient with regards to perioperative mortality and complication risks.

In comparison to the lap chole cohort, our results showed no significant difference in inpatient mortality rate with lap appy. The decision whether to proceed with surgery or attempt initial antibiotic treatment is multifactorial knowing that antibiotics may fail in 8% of patients during initial hospitalization and that approximately 20% of those patients may be hospitalized a second time for recurrent appendicitis [11].

There are several limitations to our study. First, this is a retrospective cohort study. Thus, we cannot definitively attribute cause and effect but rather we report strong and significant associations with COVID-19. In addition, our study does not stratify mortality rates by severity of COVID-19 infection. Although this data may be considered historical, we believe its uniqueness lies in capturing the pure effects of the virus when combined with general laparoscopic procedures such as cholecystectomy and appendectomy, without the confounding effects of different vaccines and subsequent strains that emerged later. We hope that the results of this manuscript can contribute to a historical compendium of surgical COVID-19 patients.

Conclusion

In this paper, we conducted a retrospective analysis of the initial wave of the COVID-19 pandemic to examine the clinical outcomes of patients with COVID-19 who underwent laparoscopic cholecystectomy or appendectomy during the pre-vaccine era. Our findings revealed that COVID-19 patients who underwent laparoscopic cholecystectomy during hospital admission had a significantly higher risk of mortality, respiratory failure, and ARDS, whereas laparoscopic appendectomy did not show the same association.

Funding/Financial support

The authors have no related funding or financial support to declare.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study [published correction appears in Lancet. 2020 Jun 9] Lancet 2020; 396(10243):27–38. https://doi.org/10.1016/S0140-6736(20)31182-X.

[2] Dshs.texas.gov. Cases and deaths by vaccination status. 2022. Available at, https://www.dshs.texas.gov/immunize/covid19/data/cases-and-deaths-by-vaccination-status-11082021.pdf.

[3] Kabir T, Kam JH, Chew MH. Cholecystectomy during the COVID-19 pandemic: current evidence and an understanding of the 'new' critical view of safety: correspondence. Int J Surg 2020;79:307–8. https://doi.org/10.1016/j.ijsu.2020.06.012.

[4] Francis N, Dort J, Cho E, et al. SAGES and EAES recommendations for minimally invasive surgery during COVID-19 pandemic. Surg Endosc 2020;34(6):2327–31. https://doi.org/10.1007/s00464-020-07565-w.

[5] Shabbir A, Menon RK, Somani J. ELSA recommendations for minimally invasive surgery during a community spread pandemic: a centered approach in Asia from widespread to recovery phases [published online ahead of print, 2020 May 11] Surg Endosc 2020:1–6. https://doi.org/10.1007/s00464-020-07618-0.

[6] El Boghdady M, Ewalds-Kvist BM. Laparoscopic Surgery and the debate on its safety during COVID-19 pandemic: a systematic review of recommendations. Surgeon 2021;19(2):e29–39. https://doi.org/10.1016/j.surge.2020.07.005.

[7] Vigneswaran Y, Prachand VN, Posner MC, Matthews JB, Hussain M. What is the appropriate use of laparoscopy over open procedures in the current COVID-19 climate? J Gastrointest Surg 2020;24(7):1686–91. https://doi.org/10.1007/s11605-020-04592-9.

[8] Coccolini F, Tartaglia D, Puglisi A, et al. SARS-CoV-2 is present in peritoneal fluid in COVID-19 patients. Ann Surg 2020;272(3):e240–2. https://doi.org/10.1097/SLA.0000000000004030.

[9] Okamoto K, Suzuki K, Takada T, et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis [published correction appears in J Hepatobiliary Pancreat Sci. 2019 Nov;26(11):534] J Hepatobil Pancreat Sci 2018; 25(1):55–72. https://doi.org/10.1002/jhbp.516.

[10] BRIEF outline of management of symptomatic gallbladder disease and acute cholecystitis during the COVID -19 pan epidemic. Facs.org. https://www.facs.org/-/media/files/covid19/symptomatic_gallbladder_recommendations.ashx.

[11] Podda M, Gerardi C, Cillara N, et al. Antibiotic treatment and appendectomy for uncomplicated acute appendicitis in adults and children: a systematic review and meta-analysis. Ann Surg 2019;270(6):1028–40. https://doi.org/10.1097/SLA.0000000000003225.

[12] Nahshon C, Bitterman A, Haddad R, Hazzan D, Lavie O. Hazardous postoperative outcomes of unexpected COVID-19 infected patients: a call for global consideration of sampling all asymptomatic patients before surgical treatment. World J Surg 2020;44(8):2477–81. https://doi.org/10.1007/s00268-020-05575-2.

[13] Fader AN, Huh WK, Kesterson J, et al. When to operate, hesitate and reintegrate: society of gynecologic oncology surgical considerations during the COVID-19 pandemic. Gynecol Oncol 2020;158(2):236–43. https://doi.org/10.1016/j.ygyno.2020.06.001.

[14] Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine 2020;21:100331. https://doi.org/10.1016/j.eclinm.2020.100331. Published 2020 Apr 5.

[15] Rasslan R, Dos Santos JP, Menegozzo CAM, et al. Outcomes after emergency abdominal surgery in COVID-19 patients at a referral center in Brazil. Updates Surg 2021;73(2):763–8. https://doi.org/10.1007/s13304-021-01007-5.