

# Hepatopancreatobiliary surgery in a Mexican social security hospital during the COVID-19 pandemic

## *Cirugía hepatopancreatobiliar en un hospital de seguridad social mexicana durante la pandemia COVID-19*

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### Abstract

**Introduction:** Data on hepatopancreatobiliary (HPB) surgery and COVID-19 are scarce. The objective of the study was to determine the outcomes HPB procedures during the COVID-19 pandemic and compare results to the previous year. **Methods:** IRB approved study of HPB procedures (April, 2020-November, 2020). Primary endpoints: Thirty-day surgical morbidity/mortality, including COVID-19 infection. Secondary endpoints: Comparison between 2019 and 2020 procedures. **Results:** Twenty-five patients were included. In 2020, HPB procedures decreased 31.6%. About 60% developed complications (Clavien-Dindo Grade III, 20%). Three patients developed post-operative COVID-19 infection (two deaths: 66% COVID-19 mortality). When compared to the previous year, there were more emergency cases, ventilator-assisted patients ( $p < 0.05$ ) and pre-operative acute renal failure ( $p = 0.06$ ). Clavien-Dindo complication grades were higher in 2020. Thirty-day mortality was also higher (16% vs. 5.6%). **Conclusion:** HPB surgical activity was negatively influenced by COVID-19 on 30-day morbidity/mortality. HPB patients who developed post-operative COVID-19 infection had a complicated course with significant mortality.

**Keywords:** Hepatopancreatobiliary. COVID-19. Outcomes.

### Resumen

**Objetivo:** Los datos sobre cirugía hepatopancreatobiliar (HPB) y COVID-19 son escasos. El objetivo del estudio fue determinar los resultados de procedimientos de HPB durante la pandemia COVID-19 y comparar resultados con el año anterior. **Material-Métodos:** Estudio de procedimientos HPB aprobado por el IRB (04/2020-11/2020). Criterios de valoración principales: morbilidad/mortalidad quirúrgica a los 30 días, incluida la infección por COVID-19. Criterios de valoración secundarios: comparación entre los procedimientos de 2019 y 2020. **Resultados:** Se incluyeron 25 pacientes. En 2020, los procedimientos de HPB disminuyeron 31.6%. El 60% desarrolló complicaciones (grado III de Clavien-Dindo, 20%). 3 pacientes desarrollaron infección posoperatoria por COVID-19, (2 muertes: 66% de mortalidad por COVID-19). En comparación con el año anterior,

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hubo más casos de emergencia, pacientes asistidos por ventilador ( $p < 0.05$ ) e insuficiencia renal aguda preoperatoria ( $p = 0.06$ ). Los grados de complicación de Clavien-Dindo fueron más altos en 2020. La mortalidad a 30 días también fue más alta (16% frente a 5.6%). **Conclusión:** La actividad quirúrgica de HPB fue influenciada negativamente por COVID-19 en la morbilidad/mortalidad a 30 días. Los pacientes con HPB que desarrollaron infección posoperatoria por COVID-19 tuvieron un curso complicado con una mortalidad significativa.

**Palabras clave:** Hepatopancreatobiliar. COVID-19. Resultados.

## Introduction

In December 2019, an outbreak of the 2019 novel coronavirus (COVID-19) caused by SARS coronavirus 2 (SARS-CoV-2) occurred in Wuhan, China<sup>1,2</sup>; spreading worldwide<sup>3</sup>, with the WHO declaring a COVID-19 pandemic on March 11, 2020. In Mexico, the first COVID-19 case was reported on February 27, 2020<sup>3</sup>. By the end of November, Mexico had 1,113,543 confirmed cases and 105,940 deaths. The state of Veracruz ranks ninth in the number of cases and the city of Veracruz ranks first in the state's number of cases<sup>4</sup>.

The COVID-19 pandemic has stressed every health system in the world. The impact on the surgical services has been profound and one of the first responses was to cease all non-essential surgical operations. Although postponing elective surgeries could help to decrease the number of exposed cases in hospital settings, the prolongation of waiting time could increase the risk of COVID-19 infection in patients with comorbidities<sup>5</sup>. Some elective surgery for time-sensitive conditions continued with prioritization of patients with resectable cancers at risk for progression and patients for whom alternative treatment modalities would be ineffective<sup>6-8</sup>.

Patients undergoing surgery are at risk of SARS-CoV-2 exposure in the hospital. They are particularly susceptible to pulmonary complications, due to pro-inflammatory cytokines, immunosuppressive response to surgery, and mechanical ventilation<sup>9</sup>. Morbidity and mortality in COVID-19 patients are higher than patients without COVID-19 infection<sup>8,10-12</sup>.

Data on the effects of COVID-19 on surgical hepatopancreatobiliary diseases (HPB) are yet to be fully reported. Until now, worldwide, HPB centers have reported a reduction in the number of surgical procedures<sup>6,7</sup>. Reported outcomes in HPB surgery during this pandemic are scarce<sup>13-16</sup>. COVID-19 might have a direct effect on HPB surgery and its outcomes due to COVID-19 infection. Furthermore, COVID-19 might

also have an indirect HPB surgery due to the decrease in health-care resources and capacity.

In view of this, the objective of this study was to determine the clinical characteristics and the outcomes of patients who underwent an HPB procedure during the COVID-19 pandemic in the regional reference social security hospital of Veracruz, Mexico, and compare their results to the previous year (2019).

## Methods

### Patient and study design

This observational study consisted of a prospectively collected database of HPB surgeries performed between April 1, 2020, and November 30, 2020, performed at Mexican Social Security reference center hospital. Procedures included in the study were as follows: (a) hepatic surgery (liver resection < 3 segments and hemi-hepatectomy); (b) pancreatic surgery (pancreatoduodenectomy, distal pancreatectomy, and pancreatic pseudocyst surgery), and (c) complex biliary surgery (bile duct injury repair and other gallbladder and bile duct surgery related to biliary/intestinal fistula). A retrospective chart review of the same procedures performed between similar dates in 2019 was performed to serve as comparison of outcomes. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The study was approved by the local ethics committee (R-2020-3001-45 and R-2021-3001-26).

The data recorded for all patients were according to the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) surgical risk calculator<sup>17</sup> with the entry of the following variables: age, sex, functional status, emergency case, American Society of Anesthesiologists (ASA) classification, steroid use, ascites, sepsis within 48 h before surgery (any of the following occurring within 48 h before surgery: systemic inflammatory response syndrome (SIRS), sepsis, and septic shock),

ventilator status, disseminated cancer, diabetes mellitus (insulin and non-insulin-dependent), hypertension, congestive heart failure, dyspnea, current smoker, severe COPD, dialysis, acute renal failure and height and weight for body mass index determination (BMI)<sup>17</sup>.

### **SARS-CoV-2 procedures**

Screening for COVID-19 infection varied on the presence of symptomatology as well as a combination of oropharyngeal swabs analyzed by real-time polymerase chain reaction (RT-PCR) and un-contrasted computed tomography (CT) of the chest. Radiological COVID-19 diagnosis based on chest CT was following CO-RADS classification<sup>18</sup>. All patients underwent a clinical respiratory triage investigating highly indicative symptoms of SARS-CoV-2 infection<sup>2</sup>, such as cough, fever, headache, myalgia, arthralgia, sore throat, nasal drip, conjunctivitis, chest pain, and dyspnea. A chest CT was performed as well. Patients underwent surgery if they were asymptomatic and were classified as CO-RADS 1 on radiological examination. Post-operative patients who developed respiratory symptoms and/or complications underwent RT-PCR and a chest CT.

### **Outcomes**

The primary endpoints of the study were 30-day surgical mortality and complications, including COVID-19 infection during hospitalization. Secondary endpoints included a comparison of primary outcomes between 2019 and 2020 patients and procedures.

Complications were defined by the Clavien-Dindo classification of surgical complications<sup>19</sup> and by the ACS-NSQIP<sup>17</sup> as follows: pneumonia, cardiac complication, surgical site infection, urinary tract infection, venous thromboembolism, renal failure, readmission, reoperation, sepsis, post-operative blood transfusion, and death.

### **Statistical analysis**

Data are expressed as mean  $\pm$  standard deviation and range for continuous variables. Categorical variables are expressed in frequency and percentage. Student's *t*-test was used to assess differences between continuous variables. Categorical variables were compared using  $\chi^2$ .  $p < 0.05$  was considered

statistically significant. Data were analyzed using SPSS software version 26 (Chicago, IL, USA).

## **Results**

Twenty-five patients ( $n = 25$ ) underwent an HPB procedure during 2020. The mean age was  $48.4 \pm 17$  years. Nineteen patients (76%) were female with a mean BMI of  $25.5 \pm 4$  kg/m<sup>2</sup>. Six patients (24%) had hypertension, 4 patients (16%) had diabetes mellitus, and 5 patients (20%) were considered an emergency case. Table 1 shows the rest of the pre-operative characteristics of the patients. The most common procedures performed during 2020 were bile duct injury repairs ( $n = 11$ , 44%) followed by hemi-hepatectomy and pancreatoduodenectomy ( $n = 4$ , 16% each, respectively) (Table 1).

According to the Clavien-Dindo classification, 15 patients (60%) developed a 30-day complication. The most common Clavien-Dindo complication was Grade III ( $n = 5$ , 20%). Thirteen patients (52%) required a post-operative blood transfusion. The most common type of complication by ACS-NSQIP was surgical site infection and pneumonia in 5 patients (20%) each. Thirty-day mortality was 16% ( $n=4$ ) (Table 2). The mean length of hospital stay was  $12.4 \pm 9.6$  days. Three patients (12%) developed post-operative COVID-19 infection, and two patients with COVID-19 died for a 66% COVID-19 mortality. Brief summary of COVID-19 patients is described in table 2.

### **Comparison between 2019 and 2020**

Thirty-six HPB surgeries were performed in 2019; therefore, the number of cases/procedures decreased by 31.6% ( $n = 11$ ). In 2020, more patients ( $n = 5$ , 20%) were considered emergency cases (the principal operative procedure must be performed during the hospital admission for the diagnosis and the surgeon and/or the anesthesiologist must report the cases as emergent) against 2019 patients ( $n = 1$ , 2.8%). In 2020, 4 patients (20%) required ventilator-assisted respiration at any time during the 48 h preceding surgery against 2019 patients ( $n = 0$ ). These differences were statistically significant. There were more patients in 2020 with pre-operative acute renal failure ( $n = 3$ , 12%) than patients in 2019 ( $n = 0$ ) but this difference did not reach statistical significance ( $p = 0.06$ ). The rest of the comparison of the demographic

**Table 1. Demographic characteristics and list of hepatopancreatobiliary procedures**

	2019	2020	p value
Age, years (mean ± SD)	50.7 ± 14.5	48.4 ± 17.4	0.5
Age group			
< 65 years	31, 86.1%	19, 76%	
65-74 years	2, 5.6%	5, 20%	
75-84 years	3, 8.3%	1, 4%	0.1
> 85 years			
Sex			
Female (n, %)	21, 58.3%	19, 76%	
Male (n, %)	15, 41.7%	6, 24%	0.1
Functional status			
Independent	34, 94.4%	22, 88%	
Partially dependent	2, 5.6%	3, 12%	0.3
Emergency case			
Yes	1, 2.8%	5, 20%	0.02*
ASA class			
Healthy patient (I)	6, 16.7%	5, 20%	
Mild systemic disease (II)	21, 58.3%	13, 52%	
Severe systemic disease (III)	8, 22.2%	5, 20%	
Severe systemic disease/ constant threat to life (IV)	1, 2.8%	2, 8%	0.7
Steroid use for chronic condition			
Yes	0, 0%	0, 0%	
Ascites within 30 days before surgery			
Yes	1, 2.8%	1, 4%	0.9
Sepsis within 48 hours before surgery			
Yes	2, 5.6%	3, 12%	0.3
Ventilator dependent			
Yes	0, 0%	4, 16%	0.013*
Disseminated cancer			
Yes	2, 5.6%	4, 16%	0.1
Diabetes			
Yes (oral medication)	11, 30.6%	4, 16%	0.1
Hypertension			
Yes	14, 38.9%	6, 24%	0.2
Current smoker within 1 year			
Yes	4, 11.1%	2, 8%	0.6
History of severe COPD			
Yes	2, 5.6%	1, 4%	0.7
Acute renal failure			
Yes	0, 0%	3, 12%	0.06
Body mass index (kg/m <sup>2</sup> ) (mean ± SD)	24.7 ± 3.5	25.5 ± 4.2	0.4
Body mass index category			
Normal (20-25 kg/m <sup>2</sup> )	23, 63.9%	16, 64%	
Overweight (25-30 kg/m <sup>2</sup> )	10, 27.8%	6, 24%	

(Continues)

**Table 1. Demographic characteristics and list of hepatopancreatobiliary procedures (Continued)**

	2019	2020	p value
Obesity (> 30 kg/m <sup>2</sup> )	3, 8.3%	3, 12%	0.8
Procedure	Number	Number	
Liver			
Liver resection<3 segments	4	2	
Hemi-hepatectomy	1	4	
Pancreas			
Pancreatoduodenectomy	7	4	
Distal pancreatectomy	4	1	
Pseudocyst surgery	1	0	
Gallbladder and bile duct			
Bile duct injury repair	15	11	
Gallbladder/bile duct surgery related to biliary/intestinal fistula	4	3	
Total	36	25	0.4

ASA: American society of anesthesiologists, COPD: chronic obstructive pulmonary disease, \*statistically significant by Chi-square.

characteristics between 2019 and 2020 is displayed in table 1.

In regard to the surgical outcomes, 2020 patients had shorter in-hospital length of stay than 2019 patients (12.4 ± 9.6 days against 14.9 ± 13. days). Although the 30-day complication rate (Clavien-Dindo) was similar between years, 2020 complications were more severe (Grade III to IV) in 2020 patients (52%) than 2019 patients (39%). Nevertheless, these differences were not statistically significant. A similar pattern was noted in 30-day mortality, in which 2020 patients were 16% against 2019 patients (5.6%) but were not statistically significant. Noteworthy, COVID-19 infection was the main cause of mortality in 2020 patients (two out of four patients, 50%). Table 3 details 30-day morbidity and mortality according to the Clavien-Dindo classification and ACS NSQIP classification.

## Discussion

The results of this study evidenced that the HPB surgical activity during the COVID-19 pandemic decreased. The results of the study also demonstrate that the 30-day morbidity and mortality of HPB surgical procedures performed during the COVID-19 pandemic was high, and even higher when compared to the previous year. Patients who underwent HPB surgery during the COVID-19 pandemic year were more considered as an emergency case and had other



**Table 2. Surgical outcomes by year**

	2019	2020	p value
Length of stay, days (mean ± SD)	14.9 ± 13.4	12.4 ± 9.6	0.4
Clavien-Dindo classification of complications			
No complications	14, 38.9%	10, 40%	0.7
Grade I	2, 5.6%	1, 4%	0.2
Grade II	5, 13.9%	1, 4%	0.4
Grade III	10, 27.8%	5, 20%	0.1
Grade IV	2, 5.6%	4, 16%	0.1
Grade V (death)	2, 5.6%	4, 16%	0.03*
COVID-19 infection	0	3, 12%	
ACS NSQIP complication			
Pneumonia	3, 8.3%	5, 20%	0.1
Cardiac complication	0	1, 4%	0.2
Surgical site infection	10, 27.8%	5, 20%	0.4
Urinary tract infection	3, 8.3%	1, 4%	0.5
Venous thromboembolism	1, 2.8%	0	0.4
Renal failure	2, 5.6%	4, 16%	0.1
Sepsis	9, 25%	8, 32%	0.5
Reintervention	4, 11.1%	4, 16%	0.5
Readmission	2, 5.6%	2, 8%	0.7
Post-operative blood transfusion	20, 55.6%	13, 52%	0.7
Death	2, 5.6%	4, 16%	0.1

\*Statistically significant by Chi-square.

ACS: American college of surgeons; NSQIP: National surgical quality improvement program.

significant pre-operative conditions against 2019 HPB surgery patients. Besides, the results of this study also corroborate that patients who developed post-operative COVID-19 infection had a complicated in-hospital course with significant mortality.

The decrease in HPB surgical activity in the COVID-19 pandemic was noticed by HPB surgeons in Europe. Different surveys reported a decrease in HPB cancer patients' referral in up to 60% compared to pre-pandemic standards<sup>6</sup>. HPB oncologic surgery was temporarily discontinued in hospitals with few HPB procedures, mostly related to hospital and intensive care bed restrictions<sup>6</sup>. Another survey conducted by the European-African Hepato-Pancreato-Biliary Association to assess the impact of COVID-19 on HPB surgery, described a 50% reduction in the operating theaters capacity, an 82% cancelation on HPB procedures if patients were COVID-19 (+), and a 90% reduction in HPB cancer procedures. Non-essential surgical procedures such as elective cholecystectomies were canceled. Interestingly, 36% did not perform COVID-19 pre-operative screening/testing<sup>7</sup>. Although we did have a decreased activity in our HPB procedures (31%) as seen in Europe, it was not as pronounced as our previously reported (79%) general and surgical oncology surgical total activity<sup>8</sup>. HPB

malignancies should be considered urgent operations due to their biological aggressive nature<sup>7</sup> and some bile duct injury repairs might not have other treatment modalities<sup>20</sup>. Similar to other HPB centers<sup>7</sup>, our hospital canceled elective cholecystectomies, and therefore, they were not included in our study.

Experience describing COVID-19 infection in patients following HPB intervention is scant and controversial. An initial case series during the initial outbreak (March 2020) in the UK described three patients, two of them most likely developed COVID-19 infection after the intervention with no mortality<sup>13</sup>. Larger case series from the UK described one case of COVID-19 infection out of 30 HPB interventions, with a 3.3% mortality and no COVID-19 related mortality<sup>14</sup>. In addition, 36 liver surgeries were managed in Iran without COVID-19 infection and no mortality<sup>16</sup>. These case series differ from reports of severe fatality in the peri-operative period in patients who developed COVID-19 infection such as series from Iran where two out of four infected patients died after surgery (non-HPB)<sup>10</sup>, or a series in a third-level specialty hospital in Lombardy (the epicenter of the Italian pandemic) with a 19.5% mortality rate in general surgery patients<sup>12</sup>, and the COVID-19 Surg multicenter cohort study in which COVID-19 (+) patients had a 23.8% 30-day mortality rate<sup>11</sup>. Another case series (n = 57) from the UK (Leicester); despite the decrease of referrals in aforementioned surveys<sup>6,7</sup>, reported a 42% increase in attempted HPB resections when their data were compared with the same period in 2019, without differences in intensive care stay, length of hospital stay, and no differences in complications (Clavien-Dindo classification) between years<sup>15</sup>. As we have previously stated, we had a decreasing number of HPB cases during this pandemic year. Interestingly, our patients had significantly worse pre-operative conditions than the previous year, therefore, our post-operative outcomes could be affected, resulting in an increment of the 30-day morbidity and mortality. In addition to this, COVID-19 infection was present in 12%, with a negative impact on the mortality as well. In the case of patients who developed COVID-19 infection, a thorough examination of each patient unveils typical conditions associated with COVID-19, such as age > 60 years, male sex, diabetes mellitus, and renal failure<sup>2,8,9</sup>. Although it is difficult to assess, two out of the three patients were likely exposed to SARS-CoV-2 while admitted to the hospital (post-operative days 6 and 8). To prevent this, COVID-19 Surg Collaborative has recently described that dedicated COVID-19-free

**Table 3. Characteristics of patients who developed COVID-19 infection**

	Gender	Age (years)	BMI (kg/m <sup>2</sup> )	Comorbidities	Procedure	Surgery date	COVID-19 diagnosis	CORADS	Assisted ventilation	Length of stay (days)	Mortality
Patient 1	Male	69	25.3	Acute renal failure, sepsis	Gallbladder/bile duct surgery related to biliary/intestinal fistula	05/06/2020	POD 5	V	Yes	19	Yes
Patient 2	Male	68	21.77	Diabetes mellitus, hypertension	Hemi-hepatectomy	25/06/2020	POD 6	V	Yes	23	Yes
Patient 3	Female	53	21.8	None	Pancreatoduodenectomy	01/07/2020	POD 8	V	No	22	No

BMI: Body mass index; CORADS: COVID-19 reporting and data system; POD: Post-operative day.

surgical pathways could be established to provide safe elective cancer surgery during SARS-CoV-2 outbreaks<sup>21</sup>. Nevertheless, the analysis of our results also reveals an indirect problem, such as hospital overcrowding in limited resources countries regarding supplies availability to handle health-care challenges during the COVID-19 pandemic<sup>22</sup>.

We must acknowledge as a major limitation to our study that is a small series number of cases coming from a single center. However, it brings valuable information on the surgical practice challenge in the COVID-19 pandemic, especially in low- and middle-income countries in Latin America. The future trajectory of the pandemic is still uncertain, and the evidence provided by our study is relevant to further preparation, development, and guidance of pre-operative and post-operative care in HPB interventions in our region.

## Conclusion

HPB surgical activity was negatively influenced by COVID-19 in terms of 30-day morbidity and mortality when compared to the previous year. Patients who underwent an HPB intervention who developed post-operative COVID-19 infection had a complicated in-hospital course with significant mortality. Significant efforts should be made to resume previous HPB surgical activity and prevent COVID-19 infection in this sub-setting of patients.

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## Conflicts of interest

The authors declare no conflicts of interest.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

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