Impact of the COVID-19 Pandemic on Gallstone Disease: Experience at a High-Volume Center

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Abstract

Background: Diagnostic delay associated to COVID-19 pandemic led patients to present with more advanced conditions than usual. The aim of this study was to analyze Laparoscopic Cholecystectomies (LC) performed for acute gallstone-related disease during the pandemic and to compare them with two control groups.

Methods: All LC performed between April and July 2020 (Group 3: G3) were analyzed and compared with LC performed in the same period in 2019 (Group 2: G2) and 2018 (Group 1: G1).

Results: In G3 80 LC were performed, of which 36 (45%) were due to acute disease, while in G1 of 192 LC 45 (23.44%) and in G2 of 234 LC 37 (15.81%) were due to acute disease (p <0.01). Time from symptom onset until hospital consultation was longer during the pandemic (G3: 3.8 days vs 2.87 days for G1 and 2.26 days for G2; p <0.05). Mean operative time in minutes was also longer: 78.56 (SD ± 31.6) for G3, 57.69 (SD ± 26.5) for G1 and 63.51 (SD ± 29.4) for G2 (p <0.01).
Discussion: We observed a significant delay in hospital consultation due to acute gallstone-associated disease resulting in more advanced cases requiring increased operative time for their resolution.

Keywords
Gallstone Disease; COVID-19 Pandemic; SARS-CoV-2; Laparoscopic Cholecystectomy; Elective Surgery

Introduction
In late December 2019, seven patients presenting with unusual pneumonia were detected in Wuhan (China) and reported to the Chinese Center for Disease Control and Prevention [1]. Since then, the disease, named COVID-19, has spread throughout the world and has been considered a pandemic since 11 March 2020 by the World Health Organization [2].

While most people with COVID-19 have only mild or uncomplicated illness, approximately 20% develop severe disease that requires hospitalization and oxygen support, and 5% need admission to an intensive care unit [1]. Considering the imbalance between infected healthcare professionals and patients, surgical societies were forced to modify their practice recommendations including rescheduling of all elective surgeries [3,4].

In addition to the above and as well as the fear of becoming infected, there has been a significant decrease in the numbers of persons seeking emergency medical care [5,6]. Based on this decrease, may be hypothesized we would expect to face more advanced conditions than usual. However, a reduction in acute care surgeries was reported in countries with high viral caseloads such as Spain and Italy [7,8].

Gallstone disease is the most common gastrointestinal disorder for which patients are admitted to hospitals in European countries [9]. The risk of developing acute complications that require hospitalization (pancreatitis, acute cholecystitis, and choledocholithiasis) is 1-3% per year [10]. In the context of COVID-19, the management of gallstones has undergone some modifications, but LC remains the gold standard [3,11].

Here we describe the delay in hospital consultation for acute gallstone-related disease combined with a decrease in scheduled LC during the COVID-19 pandemic and analyze the consequences measured in surgical time, complications, and length of hospital stay.

Methods


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All LC performed between April and July in 2018, 2019, and 2020 were included in the study. Those that were not scheduled (performed due to acute disease) were analyzed and divided into 3 groups according to year: Group 1 (G1) LC performed in 2018, Group 2 (G2) LC performed in 2019, and Group 3 (G3) LC performed in 2020. Patients with acute gallstone-related disease that underwent non-surgical treatment were excluded.

Retrospective analysis of a prospectively maintained database was conducted including: Demographic data (sex, age, body mass index (BMI), comorbidities such as diabetes and hypertension, and previous abdominal surgeries), perioperative data (form of presentation, time until consultation, complementary studies, type of approach, operative time, complications, conversions, and length of hospital stay), and postoperative data (outpatient follow-up and complications and their management).

All the patients were physically examined 7 days and one month postoperatively, and subsequently if needed with a minimum follow-up of 90 days. Complications observed during this period were classified according to the Clavien-Dindo classification [12,13].

**Therapeutic Algorithm**

During the COVID-19 pandemic, surgical treatment of acute gallstone-related disease was performed as long as the patient did not present characteristic symptoms of SARS-CoV-2 and/or had a negative reverse transcription polymerase chain reaction (RT-PCR) test from a nasopharyngeal swab. At least one operating room was always available for non-scheduled surgeries including those associated to gallstones disease. In case of positive RT-PCR test, medical rather than surgical treatment was selected as permitted by the patient's condition [4,11]. If medical therapy failed, percutaneous cholecystostomy was next considered [11,14]. Fortunately, at this series no percutaneous approach were needed since every patient that was excluded from surgical treatment resolved with medical treatment. At our center, Endoscopic Retrograde Cholangiopancreatography (ERCP) is considered the first intervention in cases of choledocholithiasis and was an alternative for those patients with cholangitis that did not resolve with antibiotic treatment.

**Surgical Technique**

LC was performed by placing 4 trocars (1 umbilical of 10 mm, 1 in the epigastrium of 5 mm, and 2 in the right flank, also 5 mm), entering the abdominal cavity using an open technique, and creating the pneumoperitoneum at 12 mm Hg. Once the gallbladder was identified and freed from its possible adhesions, the triangle of Calot was dissected and the cystic duct and the cystic artery identified, achieving Strasberg’s “critical view of safety” [15,16].
Intraoperative cholangiography was performed in cases of pancreatitis, choledocholithiasis, and when there were anatomical doubts. The artery and cystic duct were sectioned after placing proximal and distal metal clips. The gallbladder was dissected towards the vesicular fundus with electrocautery and then removed through the umbilical wound using an endobag. Hemostasis was performed with subsequent lavage and aspiration, and if the surgeon considered it necessary a Blake drain was placed at the surgical site. After exsufflation, the trocar sites were closed.

In 2020, taking measures to reduce the possible aerosolization of SARS-CoV-2 viral particles, we decided to follow different recommendations, such as: placement of an aspiration system with chlorinated solution at the epigastric trocar, minimization of the exchange of instruments between trocars, completion of the intervention in the shortest possible time, and evacuation of the pneumoperitoneum using the epigastric trocar filtering system [17-19].

All the acting medical staff used protective equipment according to the international recommendations [20] and if the clinical condition of the patient allowed for it, a PCR test was performed to detect SARS-CoV-2 before the procedure.

Statistical Analysis

Quantitative variables are expressed as means with standard deviation and range, while qualitative variables are described as percentages. Between-group comparisons were performed using the Mann Whitney and Fisher's exact tests. A p < 0.05 was considered statistically significant. Differences between the groups were evaluated by the non-parametric Kruskall Wallis and Dunn’s multiple comparison tests or by one way Analysis of Variance (ANOVA) and Bonferroni’s multiple comparison test. Analysis was performed using Prism 8.0.2 software (Graph Pad, La Jolla, CA).

Results

We analyzed the total of LC performed between April and July in 2018 (G1), 2019 (G2) and 2020 (G3) and selected those performed in context of acute gallstone-related disease. In G1, 192 LC were performed, of which 45 (23.44%) were because of acute disease; in G2, 234 LC were performed, of which 37 (15.81%) were because of acute disease; and in G3 80 LC were performed, of which 36 (45%) were because of acute disease (p <0.01), showing a significant decrease in overall scheduled surgeries but similar numbers of those performed for acute gallstone-related disease (Fig. 1).

As we can see in Table 1, demographic data including age, Body Mass Index (BMI), sex and ASA I-II distribution were similar in the three groups.


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No significant differences were found regarding the etiology of the acute disease. In G1 of 45 non-scheduled LC, 28 (62%) were due to acute cholecystitis, 10 (22%) due to acute pancreatitis, and 7 (16%) due to choledocholithiasis. In G2, of 37 non-scheduled LC, 19 (51%) were due to acute cholecystitis, 4 (11%) due to acute pancreatitis, and 14 (38%) due to choledocholithiasis. In G3, of 36 non-scheduled LC, 18 (50%) were due to acute cholecystitis, 8 (22%) due to acute pancreatitis, and 10 (28%) due to choledocholithiasis (p = 0.47, 0.33, and 0.07 respectively; Table 2).

Mean time to consultation from symptom onset of acute disease was significantly longer in the group seen during the pandemic (G3) with a delay of 3.8 days (SD ± 3.2) versus 2.87 days (SD ± 1.7) for the G1 and 2.26 days (SD ± 2.2) for G2 (p <0.05; Fig. 2). Similarly, mean operative time 78.56 minutes (SD ± 31.6) for G3 compared to 57.69 minutes (SD ± 26.5) for G1 and 63.51 minutes (SD ± 29.4) for G2 (p < 0.01; Fig. 2).

In all three groups, most surgeries were performed by second- or third-year residents as the first surgeon: G1 n=36 (80%), G2 n= 31 (83.78%), and G3 n=32 (88.89%) (p = 0.55) but always in the presence of a senior surgeon as assistant.

There was a slight upward trend in the performance of intraoperative cholangiography. In G3 16 (44.44%) were performed out of a total of 36 LC versus 15 (33.33%) in G1 out of a total of 45 LC and 12 (32.43%) in G2 out of a total of 37 LC (p = 0.48). At our center open cholecystectomies are not frequently performed. In fact, if we analyze the last 10 years out of a total of 6372 CL only 13 (0.2%) required conversion to open surgery. Luckily none of them belonged to either group conceived for this study.

Mean length of hospital stay for acute disease after LC was 2.62 days (SD ± 2.1) for G1, 2.24 days (SD ± 2.6) for G2, and 3.5 days (SD ± 3.9) for G3, an increasing trend in the latter (p = 0.17).

The following postoperative complications assessed using the Clavien-Dindo classification were observed: one GII complication in G1 (2.22%) in a patient who required antibiotic therapy because of hospital-acquired pneumonia; one GIIIB complication in G2 (2.7%) in a patient consisting of surgical injury to the bile duct occurred during LC requiring a second intervention with the placement of a biliary stent by endoscopy; two complications in G3 (5.55%), consisting of a GI complication in a patient who required the placement of a foley catheter due to acute urinary retention and a GIV complication in a patient who presented with advanced cholecystitis and developed septic shock with the removal of the infectious in the immediate postoperative period requiring intensive care including low-dose vasoactive drugs (p = 0.68; Table 3) [12,13].
Figure 1: A: Total of LC performed between April and July in 2018 (G1), 2019 (G2) and 2020 (G3). B: Non-scheduled LC performed between April and July in 2018 (G1), 2019 (G2) and 2020 (G3).

Figure 2: A: Time from symptom onset to consultation in acute disease. B: Operative time in minutes.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>G1 (n=45)</th>
<th>G2 (n=37)</th>
<th>G3 (n=36)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SD</td>
<td>50.3 ± 17.6</td>
<td>50.35 ± 16.1</td>
<td>53.56 ± 19.6</td>
<td>0.65</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Mean ± SD</td>
<td>26.9 ± 6.9</td>
<td>31.2 ± 5.9</td>
<td>28.2 ± 5.2</td>
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<tr>
<td>Male sex (%)</td>
<td>25 (55.55)</td>
<td>20 (54.05)</td>
<td>16 (44.44)</td>
<td>0.57</td>
</tr>
<tr>
<td>ASA class I &amp; II (%)</td>
<td>39 (86.67)</td>
<td>33 (89.19)</td>
<td>30 (83.33)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Table 1: Demographic data of the patients.
<table>
<thead>
<tr>
<th>Etiology of acute disease</th>
<th>G1 (n=45)</th>
<th>G2 (n=37)</th>
<th>G3 (n=36)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholecystitis (%)</td>
<td>28 (62)</td>
<td>19 (51)</td>
<td>18 (50)</td>
<td>0.47</td>
</tr>
<tr>
<td>Pancreatitis (%)</td>
<td>10 (22)</td>
<td>4 (11)</td>
<td>8 (22)</td>
<td>0.33</td>
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<tr>
<td>Choledocholithiasis (%)</td>
<td>7 (16)</td>
<td>14 (38)</td>
<td>10 (28)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

**Table 2:** Etiology of acute disease.

<table>
<thead>
<tr>
<th>Grade</th>
<th>G1 (n=45)</th>
<th>G2 (n=37)</th>
<th>G3 (n=36)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>n.d*</td>
</tr>
<tr>
<td>Grade II</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>n.d*</td>
</tr>
<tr>
<td>Grade III</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>n.d*</td>
</tr>
<tr>
<td>Grade IV</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>n.d*</td>
</tr>
<tr>
<td>Total</td>
<td>1 (2.22%)</td>
<td>1 (2.7%)</td>
<td>2 (5.55%)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

n.d*: non determined

**Table 3:** Complications based on Clavien-Dindo classification.

**Discussion**

The SARS-CoV-2 pandemic has led to reorganize the vast healthcare centers and redistribute material and human resources to face this new health issue. Surgical societies have been forced to modify their recommendations, including the rescheduling of all elective surgeries and adaptation of the surgical practice to the epidemiological context [3,4].

At our center, from the beginning of the lockdown decreed on March 20 by the government, the decision was made to cancel all non-emergency surgeries that did not meet oncological mandates. As hospital bed availability increased and viral circulation decreased, elective surgeries have been rescheduled but always under protocols that safeguard the patient and the medical staff.

When considering the total number of LC performed, the number of procedures in G3 (n=80) was far from approaching that of the same period in the previous years (n=192 for G1 and n=234 for G2; Fig. 1). This is mainly due to the decrease in scheduled surgeries, since if we only analyze the LC performed because of acute disease (pancreatitis, acute cholecystitis, and choledocholithiasis) we see the number was comparable to previous years (36 cases in G3, 45 in G1, and 37 in G2) with a similar distribution of etiologies (Fig. 1). Unlike other studies such as Cano-Valderrama, et al., [7].

Our recent total monthly LC caseload appears to be increasing. This trend is likely due to 2 reasons: on the one hand, the institutional authorization to schedule surgeries (based on an increasing number of hospital beds and less viral circulation in the community) and, on the...
other hand, a decrease in the fear of getting infected by SARS-CoV-2 when contacting the healthcare system.

As stated by Hartnett, et al., and Wong, et al., we believe that the fear of exposure to SARS-CoV-2 when visiting healthcare institutions is evidenced by the delay in medical consultation [5,6]. For acute gallstone-related disease, the mean time from symptom onset until approaching the hospital was 3.8 days in times of pandemic compared to 2.26 days in 2019 and 2.87 days in 2018 (p <0.05) (Fig. 2).

This delay has led to more advanced symptoms than usual, translated into a longer mean operative time of 78.56 minutes (SD ± 31.6) for G3 versus 57.69 minutes (SD ± 26.5) for G1 and 63.51 minutes (SD ± 29.4) for G2 (p <0.01) due to greater technical difficulty (Fig. 2). Despite we cannot underestimate the time conceded in G3 related to additional precautions to reduce the COVID-19 transmission we can assume that most of it was required as preparation before the start of the surgery (including thorough cleaning measures, additional filters for the pneumoperitoneum, increasing time between surgeries to improve ventilation, among others) not affecting substantially the operative time. Also, if we consider the time required to wear the personal protective equipment, we evidenced that for those closely related to the operating room it was much easier to get used to it. Moreover, during the COVID-19 pandemic interventions were performed as fast as possible to minimize the exposure to the virus. Even there was not statistically significantly difference at hospital stay, with a mean time of 2.62 days (SD ± 2.1) for G1, 2.24 days (SD ± 2.6) for G2, and 3.5 days (SD ± 3.9) for the G3 (p = 0.17) an upward trend was observed.

During the pandemic (G3) the only Grade IV complication occurred, consisting of a patient who delayed medical consultation (more than 72 hours), presented with advanced acute cholecystitis, and developed postoperative sepsis requiring UCI admission and vasoactive drugs. This event is similar to the case described by García Virosta M, et al., of a patient with acute cholecystitis who presented with a large liver abscess after delayed presentation to the healthcare institution [21]. We believe it is likely that both complications could have been avoided if the patients had been treated earlier.

In COVID-19-positive patients (confirmed by PCR test) or those suspected of having the infection, medical treatment was chosen as the first measure, also due to the lack of availability of operating rooms and hospital beds [4,11,14]. In agreement with Manzia, et al., we believe that during the COVID-19 pandemic, surgeons should not only take care of emergency or oncological surgeries, but also deal with benign diseases that may lead to complications if delayed resulting in a greater demand for healthcare resources [22]. Therefore, we recommend that, as long as epidemiological and institutional conditions allow elective procedures should continue but always under protocols that ensure the safety of the patient and the medical staff.
Regarding the cholecystectomy approach, we consider that a conventional approach is associated with a greater risk of surgical wound infection and eventually a longer hospital stay compared to the laparoscopic approach. Thus, we decided to continue performing LC [23,24]. Furthermore, there is no evidence of greater contagion when performing a laparoscopic approach compared to open surgery as long as certain precautions are followed [17-19]. Similar to De Simone, et al., we recommend minimizing exposure to the virus in the operating room by wearing personal protective equipment, minimizing the number of medical staff required for the surgery and reducing patient hospital stay [14,19,20]. After having performed 80 LC in times of the pandemic, no intraoperative contagion of SARS-CoV-2 was recorded.

Our study has several limitations. Firstly, our analysis was retrospective. Secondly, patients presented with acute gallstone-related disease that during the 2020 period in the context of a SARS-CoV-2 infection and received medical treatment were excluded from the study. Comparing medical with surgical treatment might be an interesting subject for upcoming studies.

**Conclusion**

We consider that the fear of becoming infected with SARS-CoV-2 caused a serious diagnostic delay of acute gallstone-related disease leading to conditions that are more advanced than those usually seen, resulting in greater technical difficulties that require a longer surgical time for their resolution.

During the pandemic, as long as epidemiological and institutional conditions allow for it, surgeons should not only take care of emergency and oncological disorders, but also deal with benign diseases that may lead to complications resulting in a greater demand of healthcare resources.

We recommend the laparoscopic approach whenever possible, taking all relevant measures to avoid contagion of patients and the health team.

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**Conflicts of Interest**
Drs. Joaquin Fernandez-Alberti, Nicolas Panzardi, Mariano Bregante, Rafael Jose Maurette, Jorge Diego Bogetti and Daniel Enrique Pirchi have no conflicts of interest or financial ties to disclose. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Ethics Approval**

Ethical approval was waived by the local Ethics Committee of the British Hospital of Buenos Aires in view of the retrospective nature of the study and all the procedures being performed as part of the routine care.

**Consent to Participate**

Due to the retrospective nature of the study, the Ethics Committee waived the requirement for written informed consent; however, all patients signed the surgical consent form.

**References**