Comparison of severity and complication rates of acute cholecystitis during pandemic and pre-pandemic periods?

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Abstract

Background: Cancellations of surgeries for elective cases and late admissions of symptomatic cases during the pandemic period might have increased the number of cases of acute cholecystitis and its complications. 

Purpose: To compare the severity of acute cholecystitis and complication rates during the pandemic and pre-pandemic periods. 

Material and Methods: We evaluated the computed tomography (CT) findings observed for the diagnosis of complications for both acute simple and acute complicated cholecystitis during both the pandemic and pre-pandemic periods. Patients admitted to the hospital between March 2020 and December 2020 made up the study group and the corresponding appropriate patients from one year earlier were studied as the control group. In addition to the CT findings, clinical and laboratory findings, co-morbidities such as diabetes, as well as the admission time to hospital from the onset of the initial symptoms to hospital admission were also evaluated. 

Results: A total of 88 patients were evaluated (54 in the study group, 34 in the control group; mean age = 64.3 ± 16.3 years). The male-to-female ratio was 51/37. The number of patients diagnosed with complicated cholecystitis were significantly higher in the study group (P = 0.03). Murphy finding and diabetes status were similar between the two groups (P = 0.086 and P = 0.308, respectively). Admission time to the hospital was significantly different for study and control groups in simple cholecystitis patients (P = 0.045); with no significant difference in cases of complicated cholecystitis (P = 0.499). 

Conclusion: Our study reveals the course of acute cholecystitis during the pandemic period was much more serious with higher complications. 

Keywords 
Complication, acute cholecystitis, perforation, pandemic, COVID-19

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Introduction

Acute cholecystitis presents with a sudden onset of upper-right quadrant pain, fever, and leukocytosis in which an impacted stone obstructing the gallbladder neck is seen in 90% of cases. Although most cases develop secondary to gallstones, in rare cases, acalculous cholecystitis may also be seen. However, this can have a more serious and complicated course due to co-morbidities. The acute form is classified into two main types: simple or complicated (1).

The contemporary approach towards defining acute cholecystitis and patient management thereof is found in the Tokyo Guidelines. A diagnosis of suspected cholecystitis is made

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with upper-right quadrant pain with fever, increased C-reactive protein (CRP) and leukocyte levels, and proven cholecystitis is diagnosed by typical imaging findings correlated with the above (2).

Although ultrasonography (US) is the gold standard modality in diagnosis, computed tomography (CT) is still frequently used to exclude other disorders with similar clinical findings such as pancreatitis, cardiac diseases, and perforations. In addition, acute cholecystitis with perforation, abscess formation, and both the emphysematous and gangrenous pattern can also be diagnosed confidently by CT (1–3).

The preferred treatment of acute cholecystitis is cholecystectomy, although percutaneous cholecystostomy and conservative antibiotic therapy may also be preferred according to a patient’s general status (1,2,4).

COVID-19 pneumonia is a viral disease that was first seen in the Wuhan province of China in December 2019 and was announced as a pandemic by the World Health Organization (WHO) in March 2020, when it spread to the entire world (5,6). Since then, tertiary healthcare facilities have served as pandemic hospitals, and elective treatments and surgeries were postponed to an unspecified date. During lockdown, patients with complaints other than COVID-19 pneumonia were told to stay at home to decrease the spread of pandemic (7). However, as might be predicted in abdominal conditions requiring immediate treatment, such as acute cholecystitis, progression of disease was inevitable to a more serious course, and even more catastrophic results were possible (4). The choice of treatment was affected by the patient’s clinical condition and co-morbidities.

The aim of the present study was to evaluate the complication rates of cholecystitis during the first year of the pandemic period.

**Material and Methods**

**Patients**

In this single-center study, we retrospectively evaluated the CT images of 54 patients admitted to the emergency department during the pandemic period between March 2020 and December 2020, given that the first case of COVID-19 was reported in our country on 11 March 2020 (8). A further 34 patients with the same diagnosis admitted to the hospital during the same time frame a year earlier were studied as the control group. All patient images were obtained from the Picture Archiving Communication Systems (PACS). The 2018 Tokyo Guidelines were used as the reference for diagnosis and treatment (2). Patients aged <18 years were excluded from the study. The study was approved by the local ethical committee (approval no. 2021-4/48).

**Classification**

The disease was classified as simple or complicated based on the CT findings. The findings—such as increased wall thickness and contrast enhancement in the gallbladder wall, inflammatory stranding of pericholecystic fatty tissue, and hydropic gallbladder—were used as the diagnostic criteria for the simple form. Additional findings—such as gallbladder wall irregularity or discontinuity, pericholecystic abscess, mucosal detachment, hemorrhage, or air in the lumen—and cholecystoenteric fistula indicated the complicated form (2,9).

**Laboratory and clinical findings**

Fever, leukocyte, neutrophil and lymphocyte counts, neutrophil to lymphocyte (N/L) ratio (10, 11), total and direct bilirubin levels (11), CRP (10), presence of Murphy finding, co-morbidities such as diabetes, time from onset to hospitalization, and treatment modalities were analyzed.

**CT technique**

The CT images were obtained with a 16-slice scanner capable of using a slice thickness of 0.75 mm (130 kvp, pitch factor: 1.5) (Somatom, Perspective; Siemens, Erlangen, Germany). All CT images were obtained at the portal venous phase following a 2–mL/kg non-ionic iodinated contrast medium injection with antecubital venous access (18–20 G). All CT images were retrospectively re-evaluated on a workstation by an experienced abdominal radiologist according to the diagnostic criteria mentioned above.

**Statistical analysis**

Continuous variables were presented as mean ± SD or median (Q1–Q3), and categorical variables as percent. The categorical variables were compared using the Pearson chi-square test or Fisher’s exact test, and odds ratios were calculated in 95% confidence intervals (CIs). The distribution of continuous variables was analyzed using the Shapiro–Wilk test, and all variables aside from age were distributed non-normally. Thus, the Mann–Whitney U test was used for comparisons. Statistical analysis was performed using SPSS version 25 software (IBM Corp., Armonk, NY, USA), and P values <0.05 were considered statistically significant.

**Results**

A total of 88 patients (51 men, 37 women; mean age = 64.3 ± 16.3 years) were included in the study (54 and 34 in the study and control groups, respectively). The other demographic characteristics are presented in Table 1. The highest frequent finding in both groups was gallbladder perforation (study group: n = 15, 27.7% vs. control group: n = 5, 14.7%) (Figs. 1–3). Other findings are presented in Table 2. The clinical and laboratory data of 75 patients were available for analysis. In 75 patients, no statistically
A significant difference in body temperature was found; however, the leukocyte count and CRP levels were significantly higher in the study group ($P = 0.036$ and $P = 0.004$, respectively). The remaining laboratory values showed no significant difference between both groups (Table 3).

A RT-PCR test was performed in 27 (50%) patients; the test was positive in two patients and negative in 25 patients. In 27 (50%) patients, COVID-19 data were not available.

The “Murphy sign” was positive in 51 cases (study group: $n = 36$, control group: $n = 15$; $P$ value = 0.086) and negative in 26 patients. The Murphy sign was not available in 11 patients (study group: $n = 5$, control group: $n = 6$). The frequencies of the Murphy sign and diabetes mellitus status were similar in both groups.

Of the 54 cases, 20 underwent a cholecystectomy and five underwent percutaneous drainage in the study group, whereas in the control group, 21 underwent a cholecystectomy and four underwent percutaneous drainage. The frequency of cholecystectomy and percutaneous drainage was higher in the control group (95% CI = 1.27–8.17, OR = 3.22; $P = 0.012$). However, the choice of percutaneous drainage and surgery was similar between the study and control groups (95% CI = 0.31–5.6, OR = 1.3; $P = 1.0$) (Table 4).

In the study group, a total of 30 patients had complicated cholecystitis and 24 had simple cholecystitis compared to 11 and 23 in the control group, respectively. There was a significant difference between the two groups regarding complication rates among acute cholecystitis patients diagnosed by CT assessments (95% CI = 1.07–6.41, OR = 2.61; $P = 0.03$). The frequency of complicated cholecystitis was also significantly higher among cases that underwent cholecystectomy in the study group (95% CI = 2.05–26.25, OR = 7.33; $P = 0.001$). The frequency of cholecystectomy and percutaneous drainage was also higher in cases with complicated cholecystitis than in patients with simple cholecystitis (95% CI = 0.11–0.67, OR = 0.27; $P = 0.004$).

Based on the CT and laboratory findings, the fever was less severe, the time to admission was shorter, and total direct bilirubin and CRP levels were lower in the control group. The mean time for admission to hospital was 48 h

Table 1. Demographic characteristics, distribution of the pandemic and non-pandemic periods, simple and complicated cholecystitis, Murphy’s finding, fever, and time to admission to hospital for the patient group.

| Murphy negative/Murphy positive* | 26/51 (13/15 control group, 13/36 study group) |
| Age (years) | 64.4 ± 16.3 |
| Simple cholecystitis/complicated cholecystitis | 47/41 |
| Non-pandemic/pandemic | 34/54 |
| Sex (F/M) | 37/51 (control group: 17/17, study group: 20/34) |
| Fever (°C) | 36.5 (36.2–37) |
| Admission time (h) | 48 (24–72) |

Values are given as n, mean ± SD, or median (range).

*11 patients were not available.
in the control group, which increased significantly to 72 h in the study group \((P = 0.014)\). Admission to the hospital was similar in both groups \((P = 0.045)\); no significant difference was observed in cases of complicated cholecystitis \((P = 0.499)\). Tables 5 and 6 present these data in detail.

**Discussion**

Advanced age and co-morbid cardiovascular diseases constitute the predominant etiologies of gangrenous cholecystitis, which is a form of complicated cholecystitis, but the...
gallbladder perforation reported in 2%–10% of cases is associated more with patients not responding to medical therapy or who experience delayed treatment (12). In cases where the gallbladder perforation develops, a temporary relief of symptoms secondary to decompression may cause a delay in the hospital admission, which also significantly increases the rate of peritonitis (13). It is reported that local gallbladder perforation was frequently present with either limited peri-cholecystic abscess (Fig. 2) or fistulization, but more generalized perforations often result in biliary peritonitis, which is associated with higher mortality rates (14). In our study, gallbladder perforation was the most frequent complication in both groups (27.7% in the study group and 14.7% in the control group).

It may be extremely difficult to identify perforation, emphysematous cholecystitis, gangrenous cholecystitis, and cholecystoenteric fistula by US (1–4).

Some speculations can be made regarding the reason for the more serious and more complicated course of the disease in study group. As underlined earlier, we think that a delay in admission to hospital due to the pandemic was the main reason. Second, the direct involvement of biliary system by the virus itself is another possibility. The virus has a primary predilection to the lung; however, possible associations of the SARS-CoV-2 virus with other pathologies such as colitis, enteritis, acute cholecystitis, acute pancreatitis, cystitis, and acute appendicitis over angiotensin-converting enzyme 2 (ACE-2) have also been reported (15). Moreover, cases of ischemic stroke, mesenteric arterial and venous thrombosis, and portal thrombosis have also been reported in the literature among cases of COVID-19 pneumonia due to the SARS-Cov-2 virus (16). There were several suspected theoretical underlying mechanisms and these included middle and small artery vasculitis, endothelial and vascular damage, increased thrombosis, and cytokine storm (17). Alongside these, two cases of acute cholecystitis were also reported among those illnesses developed during the treatment for COVID-19 pneumonia (18,19). In the first of these, Bruni et al. reported that the case had sudden-onset ischemic-hemorrhagic cholecystitis during the COVID-19 treatment, and the histopathological assessment revealed middle vessel vasculitis and arterial thrombosis on the gallbladder (18). In the second, Ying et al. reported the

### Table 3. Comparison of demographic characteristics, time to admission to hospital, and laboratory findings between patients with simple and complicated cholecystitis.

|                        | Simple cholecystitis (n = 41) | Complicated cholecystitis (n = 34) | P value |
|------------------------|-------------------------------|-----------------------------------|---------|
| Age (years)            | 61.2 ± 16.8                   | 67.7 ± 13.9                       | 0.069   |
| Fever (°C)             | 36.5 (36–36.75)               | 36.6 (36.375–37)                  | 0.106   |
| Admission time (h)     | 48 (24–72)                    | 72 (48–120)                       | 0.01    |
| WBC (K/µL)             | 10,810 (7260–14,650)          | 12,480 (9573–21,403)              | 0.036   |
| Neutrophil count (K/µL)| 7670 (4721–12,365)            | 9555 (5842–19,033)                | 0.064   |
| Lymphocyte count (K/µL)| 1438 (955–2004)               | 1355 (892–2151)                   | 0.846   |
| N/L ratio              | 5.74 (3.18–10.61)             | 7.75 (4.45–18.75)                 | 0.201   |
| Total bilirubin (mg/dL)| 1.2 (0.6–2.9)                 | 0.9 (0.5–2.7)                     | 0.496   |
| Direct bilirubin (mg/dL)| 0.5 (0.2–2.1)               | 0.5 (0.2–1.6)                     | 0.785   |
| CRP (mg/L)             | 23.6 (4.8–85.8)               | 55.1 (20.5–145.9)                 | 0.004   |

Values are given as mean ± SD or median (range). P values <0.05 were considered statistically significant.

*Time to admission and laboratory findings were not available for 13 patients.

CRP, C-reactive protein; N/L, neutrophil/lymphocyte; WBC, white blood cell.

### Table 4. Comparisons of simple and complicated cholecystitis, pandemic and non-pandemic periods, diabetes mellitus, Murphy positivity, surgery, percutaneous drainage, and observation rates.

|                                          | P value | OR       | 95% CI   |
|------------------------------------------|---------|----------|----------|
| Simple cholecystitis vs. complicated cholecystitis |         |          |          |
| Control vs. study group                   | 0.03    | 2.61     | (1.07–6.41) |
| Diabetes mellitus status                  | 0.3     | 1.78     | (0.59–5.4)  |
| Murphy test                              | 0.17    | 1.96     | (0.74–5.22) |
| Surgery and drainage vs. observation      | 0.004   | 0.27     | (0.11–0.67) |
| Non-pandemic vs. pandemic                 |         |          |          |
| Simple or complicated cholecystitis according to surgery | 0.001  | 7.33     | (2.05–26.25) |
| Surgery and drainage vs. observation      | 0.012   | 3.22     | (1.27–8.17) |
| Surgery vs. drainage                      | 1.0     | 1.31     | (0.31–5.6)  |

P values <0.05 are considered statistically significant.

CI, confidence interval; OR, odds ratio.
development of acalculous cholecystitis during the COVID-19 treatment (19). Furthermore, Balaphas et al. reported in their case that COVID-19 pneumonia could present with findings such as acute cholecystitis, and the underlying mechanism may be associated with the detected ACE-2 enzyme, to which the SARS-CoV-2 virus has an affinity, and viral RNA in the hepatocytes and the gallbladder wall. Notably, as Balaphas et al. reported, patients with upper-right quadrant pain without pulmonary findings may delay their admission out of fear of exposure to other patients who might have COVID-19. Patients may think their situation is related to a gastrointestinal condition and choose to wait for hospital treatment, resulting in further complicated underlying cholecystitis (20).

There are several reports in the literature comparing the findings between non-pandemic and pandemic periods in simple and complicated cholecystitis cases separately. Isherwood et al. compared 2019 and 2020 in their study and published a study in Spain (23). We also found that the frequencies of the complications due to delayed diagnosis and access to treatment (22). Furthermore, Valderrama et al. reported a 58.9% decrease in the number of acute surgeries in their multicenter study in Spain (23). We also found that the frequencies of the development of acalculous cholecystitis during the COVID-19 treatment (19). Furthermore, Balaphas et al. reported in their case that COVID-19 pneumonia could present with findings such as acute cholecystitis, and the underlying mechanism may be associated with the detected ACE-2 enzyme, to which the SARS-CoV-2 virus has an affinity, and viral RNA in the hepatocytes and the gallbladder wall. Notably, as Balaphas et al. reported, patients with upper-right quadrant pain without pulmonary findings may delay their admission out of fear of exposure to other patients who might have COVID-19. Patients may think their situation is related to a gastrointestinal condition and choose to wait for hospital treatment, resulting in further complicated underlying cholecystitis (20).

There are several reports in the literature comparing the diseases in the periods before and after the pandemic. Surek et al. reported a 59% decrease in emergent surgeries during the pandemic, and these were mostly incarcerated hernias, non-complicated acute appendicitis, and acute cholecystitis (21). Reichert et al. conducted a study with surgeons of the World Society of Emergency Surgery (WSES) and reported fewer acute surgeries during the pandemic and increased complications due to delayed diagnosis and access to treatment (22). Furthermore, Valderrama et al. reported a 58.9% decrease in the number of acute surgeries in their multicenter study in Spain (23). We also found that the frequencies of the cholecystectomies and percutaneous drainages were lower compared to the non-pandemic period in our hospital (95% CI = 1.27–8.17, OR = 3.22). Patients’ hesitancy in going to hospital for non-COVID-19 reasons to avoid SARS-Cov-2 infection, the almost full occupancy of hospitals with COVID-19 patients, and the postponing of elective surgeries may explain the increased complication rates (23). Isherwood et al. compared 2019 and 2020 in their study and

### Table 5. Comparisons of demographic and laboratory findings between the control and study groups.

|                  | Control group (n = 27) | Study group (n = 48) | P value |
|------------------|------------------------|----------------------|---------|
| Age (years)      | 61 (46–80)             | 65 (56–75)           | 0.893   |
| Fever (°C)       | 36 (36–36.7)           | 36.6 (36.5–37)       | 0.002   |
| Admission time (h)| 48 (24–72)            | 72 (48–90)           | 0.014   |
| WBC (K/µL)       | 10460 (6340–14590)     | 11730 (7833–19300)   | 0.076   |
| Neutrophil count (K/µL) | 7500 (4620–12330)   | 9555 (5704–15813)    | 0.12    |
| Lymphocyte count (K/µL) | 1440 (908–2147)     | 1326 (920–2065)      | 0.751   |
| N/L ratio        | 5.7 (2.8–9)            | 7.3 (4.1–14.7)       | 0.335   |
| Total bilirubin (mg/dL) | 0.7 (0.55–1.6)        | 1.6 (0.63–3.63)      | 0.047   |
| Direct bilirubin (mg/dL) | 0.3 (0.2–0.6)         | 0.75 (0.3–2.6)       | 0.022   |
| CRP (mg/L)       | 28.8 (5.1–73.8)        | 35.2 (19.2–140.8)    | 0.031   |

*P* values <0.05 are considered statistically significant.

CRP, C-reactive protein; N/L, neutrophil/lymphocyte; WBC, white blood cell.

### Table 6. Comparisons of demographic and laboratory findings between non-pandemic and pandemic periods in simple and complicated cholecystitis cases separately.

|                  | Simple cholecystitis | Complicated cholecystitis |
|------------------|----------------------|---------------------------|
|                  | Control (n = 19)     | Study (n = 22)            | P value |
| Age (years)      | 57 (44–65)           | 64 (55–76)                | 0.475   |
| Fever (°C)       | 36.2 (36–36.6)       | 36.6 (36.5–37)            | 0.011   |
| Admission time (h)| 36 (24–48)           | 60 (24–72)                | 0.045   |
| WBC (K/µL)       | 9960 (6340–14,590)   | 11175 (7598–15,773)       | 0.413   |
| Neutrophil count (K/µL) | 7500 (4162–12,330)  | 8141 (5430–14,005)        | 0.351   |
| Lymphocyte count (K/µL) | 1450 (908–2215)     | 1326 (957–1845)           | 0.762   |
| N/L ratio        | 5.7 (2.7–9)          | 5.8 (3.9–12)              | 0.546   |
| Total bilirubin (mg/dL) | 0.7 (0.6–2.2)       | 1.8 (0.7–3.5)             | 0.181   |
| Direct bilirubin (mg/dL) | 0.3 (0.2–1.3)      | 0.9 (0.3–2.5)             | 0.094   |
| CRP (mg/L)       | 23.6 (2.4–35)        | 25.5 (6–171)              | 0.094   |

|                  | Control (n = 8)      | Study (n = 26)           | P value |
| Age (years)      | 61 (46–80)           | 65 (56–75)                | 0.141   |
| Fever (°C)       | 36.6 (36.5–37)       | 36.6 (36.5–37)            | 0.269   |
| Admission time (h)| 36 (24–48)           | 60 (30–108)               | 0.499   |
| WBC (K/µL)       | 9555 (5704–15813)    | 72 (48–132)               | 0.499   |
| Neutrophil count (K/µL) | 14190 (8175–21,403) | 10,760 (7149–19,033)      | 0.55    |
| Lymphocyte count (K/µL) | 1326 (920–2065)    | 11175 (7598–15,773)       | 0.406   |
| N/L ratio        | 5.7 (2.7–9)          | 5.8 (3.9–12)              | 0.546   |
| Total bilirubin (mg/dL) | 0.7 (0.6–2.2)       | 1.8 (0.7–3.5)             | 0.181   |
| Direct bilirubin (mg/dL) | 0.3 (0.2–1.3)      | 0.9 (0.3–2.5)             | 0.094   |
| CRP (mg/L)       | 23.6 (2.4–35)        | 25.5 (6–171)              | 0.094   |

*P* values <0.05 are considered statistically significant.

CRP, C-reactive protein; N/L, neutrophil/lymphocyte; WBC, white blood cell.
reported that while the number of admissions due to cholecystitis was lower, the gallbladder perforation rate was similar (24). However, we found that the complication rates in CT assessments were significantly higher in the study group (study group: n = 30/54, control group: n = 11/34; P = 0.03). The waiting time before admission to hospital was significantly higher during the pandemic period among patients with simple cholecystitis. Nevertheless, the waiting time before admission was similar between the study and control groups for cases of complicated cholecystitis. This was thought to be associated with the fact that patients with cases of simple cholecystitis delayed their admissions, whereas patients with complicated cases (possibly with more severe pain and a deteriorated general status) went to hospital immediately. Our findings support our hypothesis. We also speculate that delayed admissions even among cases of simple cholecystitis are associated with higher complication rates.

The present study has some limitations. These include a low number of cases and the retrospective design of the study. In addition, we could not evaluate the association between the SARS-CoV-2 virus and gallbladder disease due to low number of cases of COVID-19 in our study. Further studies performed with more patients and with a prospective design may provide explanation to some questions. Our study indicates a need for further studies to show whether any correlation is present between SARS-CoV-2 and gallbladder disease.

In conclusion, it seems a delay in admission to hospitalization for simple cholecystitis during the pandemic period compared to admission time in the pre-pandemic period led to more serious cases of cholecystitis at diagnosis. This may be the main reason for the complication rates. Timely conduct of CT studies is required for cases with suspected complicated cholecystitis since it is superior to US in assessing the complications in acute cholecystitis, making early diagnosis and treatment available before the complications developed.

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References
1. Patel NB, Oto A, Thomas S. Multidetector CT of emergent biliary pathologic conditions. Radiographics 2013;33:1867–1888.
2. Yokoe M, Hata J, Takada T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci 2018;25:41–54.
3. Harvey RT, Miller WT. Acute biliary disease: initial CT and follow-up US versus initial US and follow-up CT. Radiology 1999;213:831–836.
4. Campanile FC, Podda M, Arezzo A, et al. Acute cholecystitis during COVID-19 pandemic: a multisocietary position statement. World J Emerg Surg 2020;8:15–38.
5. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
6. Available at: https://covid19.who.int (accessed 22 July 2021).
7. Cao W, Fang Z, Hou G, et al. The psychological impact of the COVID-19 epidemic on college students in China. Psychiatry Res 2020;287:112934.
8. Available at: https://covid19.saglik.gov.tr/Eklenti/39551/0/covid-19rehberigenelbiligileredemiyolojiyoljetanipdf.pdf (accessed 22 July 2021).
9. De Vargas MM, Lanciotti S, De Cicco ML, et al. Imaging delle colecistiti acute semplici e complicate [imaging of simple and complicated acute cholecystitis]. Clin Ter 2006;157:435–442.
10. Beliaev AM, Angelo N, Booth M, et al. Evaluation of neutrophil-to-lymphocyte ratio as a potential biomarker for acute cholecystitis. J Surg Res 2017;209:93–101.
11. Mahmood F, Akingboye A, Malam Y, et al. Complicated acute cholecystitis: the role of C-reactive protein and neutrophil-lymphocyte ratio as predictive markers of severity. Cureus 2021;13:e13592.
12. Ausania F, Guzman SS, Alvarez GH, et al. Gallbladder perforation: morbidity, mortality and preoperative risk prediction. Surg Endosc 2015;29:955–960.
13. Jones MW, Genova R, O’Rourke MC. Acute cholecystitis. 2021. Available at: https://www.ncbi.nlm.nih.gov/books/NBK459171/.
14. Indar AA, Beckingham IJ. Acute cholecystitis. BMJ 2002;325:639–643.
15. Lui K, Wilson MP, Low G. Abdominal imaging findings in patients with SARS-CoV-2 infection: a scoping review. Abdom Radiol 2021;46:1249–1255.
16. Azouz E, Yang S, Monnier-Cholley L, et al. Systemic arterial thrombosis and acute mesenteric ischemia in a patient with COVID-19. Intensive Care Med 2020;46:1464–1465.
17. De Roquetaillade C, Chousterman BG, Tomasoni D, et al. Unusual arterial thrombotic events in COVID-19 patients. Int J Cardiol 2021;323:281–284.
18. Bruni A, Garofalo E, Zucalà V, et al. Histopathological findings in a COVID-19 patient affected by ischemic gangrenous cholecystitis. World J Emerg Surg 2020;15:43.
19. Ying M, Lu B, Pan J, et al. COVID-19 with acute cholecystitis: a case report. BMC Infect Dis 2020;20:437.
20. Balaphas A, Gkoufka K, Meyer J, et al. COVID-19 can mimic acute cholecystitis and is associated with the presence of viral RNA in the gallbladder wall. J Hepatol 2020;73:1566–1568.
21. Surek A, Ferahman S, Gemici E, et al. Effects of COVID-19 pandemic on general surgical emergencies: are some emergencies really urgent? Level I trauma center experience. Eur J Trauma Emerg Surg 2021;47:647–652.
national survey among WSES members. World J Emerg Surg 2020;15:64.

23. Cano-Valderrama O, Morales X, Ferrigni CJ, et al. Acute care surgery during the COVID-19 pandemic in Spain: changes in volume, causes and complications. A multicentre retrospective cohort study. Int J Surg 2020;80:157–161.

24. Isherwood J, Karki B, Chung WY, et al. Outcomes of gallstone complications during the COVID pandemic. Br J Surg 2021;108:29–30.