Clinical approach to patients admitted to the emergency room due to acute cholecystitis during the COVID-19 pandemic and percutaneous cholecystostomy experience

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ABSTRACT

BACKGROUND: Acute cholecystitis (AC), a common complication of gallstones, is responsible for a significant part of emergency applications, and cholecystectomy is the only definitive treatment method for AC. Early cholecystectomy has many reported advantages. Operation-related morbidity and mortality have increased during the COVID-19 pandemic. In this study, our aim is to present our general clinical approach to patients who were diagnosed with AC during the pandemic and our percutaneous cholecystostomy experience during this period.

METHODS: This study included 72 patients who were presented to our hospital’s emergency room between March 11 and May 31, 2020, with AC. Patients were divided into three groups based on their treatment: outpatients (Group 1), inpatients (Group 2) and patients undergoing percutaneous cholecystostomy (Group 3). These three groups were compared by their demographic and clinical characteristics.

RESULTS: There were 36 (50%) patients in Group 1, 25 (34.7%) patients in Group 2, and 11 (15.3%) patients in Group 3. The demographic characteristics of the patients were similar. The CRP and WBC levels of the patients in Group 3 were significantly higher compared to the other groups. Moreover, the wall of the gallbladder was thicker and the size of the gallbladder was larger in Group 3. Patients had percutaneous cholecystostomy at the median of 3.5 days and the length of hospital stay was longer compared to Group 2 (3.9 days versus 9.2 days, p=0.00). The rate of re-hospitalization after discharge was similar in Group 2 and Group 3, but none of the patients in Group 1 required hospitalization. None of 72 patients developed an emergency condition requiring surgery, and there was no death.

CONCLUSION: Although many publications emphasize that laparoscopic cholecystectomy (LC) can be performed with low morbidity at the first admission in acute cholecystitis, it is a clinical condition that can be delayed in the COVID-19 pandemic and other similar emergencies. Thus, percutaneous cholecystostomy should be effectively employed, and its indications should be extended if necessary (e.g., younger patients, patients with lower CCI or ASA). This approach may enable us to protect both patients and health-care professionals that perform the operation from the risk of COVID-19.

Keywords: COVID-19; acute cholecystitis; percutaneous cholecystostomy.


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INTRODUCTION

Acute cholecystitis (AC), which is a common complication of gallstones, is responsible for a significant part of emergency applications, and cholecystectomy is the only definitive treatment method for AC.[1] Performing cholecystectomy at initial presentation for AC is associated with reduced long-term biliary complications, a shorter total length of hospital stay, and lower overall treatment costs.[2–5]

According to the recommendations of the “Tokyo Guidelines for Acute Cholecystitis” which was published in 2013 and revised in 2018, laparoscopic cholecystectomy is recommended for patients with mild to severe AC who have a Charlson Comorbidity Index (CCI) score of ≤5 and an American Society of Anesthesiologists physical status classification (ASA-PS) ≤2. In moderate to severe cholecystitis, it is also recommended to perform laparoscopic cholecystectomy at the first hospitalization by experienced teams. On the other hand, in patients that meet the criteria of CCI>5 and ASA-PS>2, delayed/elective cholecystectomy may be appropriate after suitable antibiotic therapy.[6–8] However, it should be kept in mind that cholecystitis recurrence or other complications related to gallstone may develop during that waiting period.[9]

In high-risk elderly patients, percutaneous cholecystostomy (PC) can be preferred as a bridge treatment before cholecystectomy, and definitive surgery can be performed in the early or late period.[10] On March 11, 2020, the World Health Organization (WHO) declared the novel coronavirus disease 2019 (COVID-19) a global pandemic, which classifies the outbreak as an international emergency, and suggested delaying all possible interventional procedures and surgeries except for very emergency cases.[11]

The risk of perioperative SARS-CoV-2 infection increases in patients who undergo surgery during this pandemic period, and it significantly increases mortality with pulmonary complications.[12] The American College of Surgeons advised in its COVID 19: Elective Case Triage Guidelines that LC should be performed to shorten the length of hospital stay in healthy young patients diagnosed with AC, and that if the patient is at high risk or operating room conditions are not suitable, antibiotics should be administered and, if this treatment is unsuccessful, PC should be applied.[13]

In this study, we aim to present our general clinical approach to patients who presented to our emergency room with the complaint of abdominal pain and were diagnosed with AC during the pandemic period, and our PC experience in these patients.

MATERIALS AND METHODS

All patients over 18 years of age who were admitted to the Fatih Sultan Mehmet Training and Research Hospital Emergency Room between March 11, 2020, and May 31, 2020, due to abdominal pain and diagnosed with AC were included in this study.

Diagnosis of Acute Cholecystitis

The diagnosis of AC was made according to the Tokyo Guidelines 2013 and 2018 (TG13/18), namely in the presence of at least one sign of local and systemic inflammation accompanying the imaging results. As imaging methods, we used abdominal ultrasonography (US) or abdominal computed tomography (CT) performed with an intravenous contrast agent. In both imaging methods, the thickness of the gallbladder wall >5 mm (wall thickness measurements from 4 to 5 mm were considered mild AC in the presence of clinical and physical examination findings), presence of pericholecystic fluid, subserosal edema on the wall of the gallbladder or Murphy’s sign in sonography were considered significant findings.

Local inflammation signs considered positive were as follows: Murphy’s sign on physical examination (palpation of the inflamed gallbladder lobe causing the patient to feel so much pain that s/he stops breathing), presence of a mass, tenderness or pain in the right upper quadrant.

Systemic inflammation signs considered significant were as follows: body temperature over 38 degrees, C-reactive protein (CRP) >3 mg/dL and leukocyte count >10000 mm<sup>3</sup>/dL.

Inclusion Criteria

1- All patients over 18 years of age who were admitted to the emergency room between March 11 and May 31, 2020, with complaints of abdominal pain and were diagnosed with AC according to the examination of the General Surgery Department in line with the Tokyo Guidelines.

Exclusion Criteria

1- Patients with acute cholangitis or acute pancreatitis accompanying AC (3-fold elevated amylase or lipase levels, stones in the main bile duct, total bilirubin level >3 mg/dL).

2- Patients who were admitted to the intensive care unit due to accompanying COVID-19 infection or those whose hospital stay continued longer than expected because of COVID-19 infection.

3- Patients whose data were not accessible in the patient’s files.

Study Design

Patients with AC were divided into three groups as follows:

**Group 1 (Outpatients)**

Outpatients were the patients who were decided to be treated and followed up in the outpatient department after the evaluation of the clinical and laboratory findings in the
emergency room. Patients were discharged from the hospital if there was pain regression after the first treatment in the emergency room and unless there was a condition hindering oral intake or patients coming to an outpatient clinic for follow-up.

**Group 2 (Inpatients)**

Inpatients were the patients who were decided to be treated and followed up in the inpatient setting isolated from COVID-19 wards after the evaluation of the clinical and laboratory findings in the emergency room. Patients who had a concomitant suspected or confirmed COVID-19 infection were taken to and followed up at the pandemic ward.

**Group 3 (Patient group undergoing percutaneous cholecystostomy)**

If patients in Group 2 did not respond to medical therapy and required PC, they were enrolled in Group 3.

**Percutaneous Cholecystostomy Technique**

The patients were placed in a semi-left lateral decubitus position and a US-guided transhepatic approach was applied. For all patients, firstly, the gallbladder was entered for 15–20 cm with an 18G needle, which was advanced through the liver segments 5 and 6, and a bile sample was collected. Later, an 8F pigtail drainage catheter (Flexima, Boston Scientific, USA) was inserted with the Seldinger technique and its location was confirmed.

**Data Collection**

Patient files were retrospectively analyzed. For file analysis, we used the International Classification of Diseases (ICD-10 Codes K80.0, K80.1, K80.4, K81.0, K81.8, K81.9) Codes. The following parameters were investigated and recorded in Excel files: age, gender, comorbid diseases (Diabetes mellitus (DM), hypertension (HT), Coronary Artery Disease (CAD), chronic kidney failure (CRF), chronic obstructive pulmonary disease (COPD), cerebrovascular disease (CVD)); body temperature, systolic and diastolic blood pressure levels, heart rate, and pulse oximeter value at first presentation to the emergency room; physical examination findings (sensitivity, the Murphy’s sign), laboratory findings (C-reactive protein (CRP), creatinine, alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), total and direct bilirubin, amylase, lipase, White Blood Count (WBC) and platelet count); Grade I (Mild), grade II (Moderate) and grade III (Severe) disease severity determined using the TG-13/18 severity indexes; diagnostic imaging method and imaging results (wall thickness, distension and size of gallbladder, pericholecystic fluid or edema, presence of stones in the bladder), number of days of hospitalization, case of re-hospitalization, suspected or confirmed COVID-19 infection. Patients’ Charlson Comorbidity Index (CCI) scores were calculated with these data. For patients in Group 2 and Group 3, the blood tests mentioned above were re-evaluated 48 hours later following hospitalization.

The groups were compared regarding their demographic data, clinical and laboratory test results, length of hospital stay, and re-hospitalization rate.

**Approval of the Ethics Committee**

For the present study, we obtained Scientific Research Approval from the Ministry of Health and the Fatih Sultan Mehmet Training and Research Hospital Ethics Committee (date: 26/06/2020, protocol no: 17073117-050,06).

**Statistical Analysis**

A statistical software package (SPSS 21 Inc., Chicago, IL, USA) was used for biostatistical analyses. The data obtained from the patients participating in this study were expressed as mean and standard deviation values and in percentages where appropriate. The distribution of the data was checked using the Kolmogorov-Smirnov test. The One-way ANOVA test was employed for the comparison of parametric data between three independent groups. For variables for which the homogeneity test (the Levene test) gave nonsignificant results, those values were considered parametric and the analysis was continued using the ANOVA test. The Bonferroni test was used in the postHoc analysis. Nonparametric tests were performed using the Kruskal-Wallis H test. In the presence of a difference between the three groups, a new p-value was determined with Bonferroni correction (p=0.017). For values that were significant according to this, new p-value were subjected to analysis using the Mann-Whitney U test. Categorical groups were compared using the Chi-Square test.

**RESULTS**

From March 11, 2020, to May 31, 2020, 72 patients were diagnosed with and treated for AC at the Fatih Sultan Mehmet Training and Research Hospital Emergency Room. Of those patients, 36 (50%) were suitable for outpatient care (Group 1), whereas the resting 36 patients were admitted to the hospital for treatment. While 25 (34.7%) patients were administered inpatient conservative therapy (Group 2), 11 (15.3) patients underwent PC performed by an interventional radiologist (Group 3).

The average age of the study population was 57.3 years, being 54.3, 57.6, and 67.0 years for Group 1, Group 2, and Group 3, respectively. When the gender distribution of the patients was examined, it was observed that 55.5% were women and the distribution in the groups was similar. When it came to comorbid diseases, 62.5% of the whole study population had at least one concomitant disease and this rate was 55.6% in Group 1, 68.0% in Group 2, and 72.7% in Group 3. Table 1 shows the details of the demographic characteristics of the patients.

Table 2 shows the results of physical examination and vital signs at the initial presentation to the emergency room.
According to these data, all patients had tenderness in the right upper quadrant and 68.1% of all patients had Murphy's sign. That percentage was 58.3%, 76.0%, and 81.8% for Groups 1, 2, and 3, respectively, and the inter-group difference was not statistically significant (p=0.2). At admission to the emergency room, 18 (25.0%) patients had a body temperature of over 38 degrees. The groups were similar concerning systolic and diastolic blood pressure and pulse rate, whereas there was a significant difference between Group 1 and Group 3 in saturation levels (p=0.04).

Patients’ laboratory test results are indicated in Table 3. The baseline CRP values of Group 3 were higher than those of the other two groups. Moreover, WBC levels of the PC group was significantly higher compared to the outpatient group (p=0.02).

Table 4 indicates imaging results and the TG13/18 AC severity classification. Accordingly, while the IV contrasted CT examination method was applied to 72.2% of the patients, ultrasound imaging was used in 34.7% of the patients for diagnosis. The wall of the gallbladder was thicker, and the size of it was larger in Group 3 patients. Considering the severity of AC, 52.8% of the patients had TG13/18 mild cholecystitis and 72.7% of the patients in Group 3 had TG13/18 severe cholecystitis.
After the diagnosis of AC in the emergency room, 36 patients (50% of the total number of patients) were hospitalized and administered IV antibiotics and fluid support as the pain did not stop, they could not have sufficient oral intake or had accompanying organ dysfunctions. Table 5 shows laboratory results at the 48th hour after hospitalization of Group 2 and Group 3, the number of days that patients spend at a hospital, and the rate of re-hospitalization after discharge. According to that table, the levels of CRP, ALT, AST, total bilirubin, direct bilirubin, and WBC were significantly higher in the PC group. The mean length of stay was 3.9 days (2–15 days) in Group 2, whereas that period extended to 9.2 days (6–20 days) when PC was applied. In both groups, the re-hospitalization rate was similar.

PC was performed for 11 patients in Group 3 after a median of 3.55 days (2–10 days) of hospitalization. We observed the growth of Escherichia coli in bile cultures of nine patients and the growth of streptococcus mutants in the cultures of two patients, and those patients were administered treatment according to the antibiogram. All patients’ laboratory results regressed after PC (at the 48th hour after PC, the median CRP
17.2, and WBC 13700), and all patients were discharged without a problem. None of 72 patients developed an emergency condition requiring surgery, and there was no case of mortality.

**DISCUSSION**

During the COVID-19 pandemic period, 72 patients were diagnosed with AC in the emergency room, and half of the patients were treated in an inpatient setting. None of the patients required emergency surgery during that period. However, 11 (15.2%) patients underwent PC. Thirty-six inpatients were discharged without complications, but three (8.3%) patients were re-hospitalized due to the complaints of pain and fever. In patients followed up in the outpatient clinic, no pathology that would require hospitalization.

Gallstones affect approximately 10% to 15% of the adult population in the US and Europe, and the incidence of complicated/asymptomatic gallstones is 14% yearly.[14] Acute calculous cholecystitis is the second most common gallstone complication after biliary colic, and laparoscopic cholecystectomy is the most frequently preferred method in its treatment.[15]

There are many studies in the literature supporting emergency surgery in AC, and the World Emergency Surgery Association (WSES) guidelines also emphasize that early laparoscopic cholecystectomy should be performed as soon as possible but can be safely performed up to 10 days of onset of symptoms.[16] However, earlier surgery is associated with a shorter hospital stay, lower need for the transition to open surgery from laparoscopy, fewer surgery-related complications along with positive effects on operational costs.[16,17]

Although there is no comprehensive study in our country reporting emergency surgery rates in AC, these are studies supporting that cholecystectomy does not increase complications and shorten hospital stay.[19,20] In our retrospective screening in our clinic, the rate of cholecystectomy was approximately 30.9% (26 of 84 patients) at the initial admission.

As we have mentioned before, the Tokyo Guidelines recommend performing cholecystectomy to patients with mild to moderate cholecystitis, which is defined as CCI ≤5 and ASA-PS ≤2.[8] Although 97.2% of our patients had CCI ≤5, we preferred a non-operative approach for all patients because of the COVID-19 pandemic. The fact that our hospital's operating room was simultaneously serving COVID-19 patients and that AC treatment can be postponed impacted our approach.

An article published to protect surgical teams during the COVID-19 outbreak reported that the virus had been found in gastrointestinal tissues, peritoneal fluid, blood, and feces, as well as in nasopharyngeal swab, sputum or tracheal aspirate. It is uncertain whether the surgical team is exposed to aerosolized viral particles during laparoscopy, but high-speed surgical equipment, such as carbon dioxide insufflation devices and energy devices, are known to produce a significant amount of aerosols.[21,22] Given this situation, we found it inappropriate to perform laparoscopic cholecystectomy in patients admitted to our clinic due to the diagnosis of AC.

Wuhan University reported that 34 patients underwent different surgeries during the COVID-19 incubation period, and 44.1% of those patients needed intensive care, with a mortality rate of 20.5%.[23]

It was reported in the international study of the COVID-Surg Collaborative group that 26.1% of 1128 patients who underwent surgery during the COVID-19 pandemic developed COVID-19 infection, and while approximately half of

| Table 5. Laboratory values on 48th hour of hospitalization of the patients in Group 2 and 3, length of stay and re-hospitalization rates |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Group 2 (n=25)  | Group 3 (n=11)  | p               |
| C-reactive protein (CRP) (mg/L) | 5.7 | 24.1 | 0.00*            |
| Creatinine (mg/dL)               | 0.90 | 1.14 | 0.11*            |
| Alanine Transaminase (ALT) (IU/L) | 45.5 | 68.2 | 0.04*            |
| Aspartate transaminase (AST) (IU/L) | 36.4 | 60.6 | 0.04*            |
| Alkaline Phosphatase (ALP) (IU/L) | 153.8 | 197.6 | 0.20*            |
| Bilirubin total (mg/dL)          | 0.75 | 1.71 | 0.00*            |
| Bilirubin direct (mg/dL)         | 0.29 | 1.06 | 0.00*            |
| White blood count (WBC) (×10⁹/L) | 9.2  | 18.6 | 0.00*            |
| Length of hospital stay          | 3.9 (2–15 day) | 9.2 (6–20 day) | 0.00*            |
| Re-hospitalization rate          | 2/25 (% 8.0)  | 1/11 (% 9.1)  | 0.67*            |

*One-way ANOVA, *Pearson Chi-Square.
those patients (51.2%) developed pulmonary complications and 23.8% of them lost their lives. The COVIDSurg Collaborative group emphasizes that the risk is higher, especially in men aged 70 and older and that emergency surgery thresholds should be higher than normal thresholds in this patient group normal practice. It should be considered to postpone non-emergency surgeries and non-surgical treatment should be encouraged to delay or prevent the need for surgery. 

Published case reports in the literature state that COVID-19 infection may manifest itself with right upper quadrant pain, high fever, elevated WBC, and thickening of the gallbladder wall in the ultrasound image. In the case report of a 45-year-old woman published in Italy, the woman underwent emergency laparoscopic surgery with this preliminary diagnosis. It was understood that she had COVID-19 infection and five healthcare workers who were in contact with the patient got infected but healed without any problems. Therefore, it would be reasonable to prefer conservative methods in AC treatment during the pandemic. First of all, antibiotic therapy and in case of no response, PC should be preferred. During the COVID-19 crisis, the indications of this minimally invasive treatment can be extended to avoid interventions, including the need for surgery and intensive care. In our patient group, we preferred PC instead of surgery in 11 patients who did not respond to antibiotic treatment and discharged all our patients without a problem.

In our study group, there was no patient diagnosed with gangrenous cholecystitis, which was a contraindication for PC. However, laparoscopic cholecystectomy was performed in three patients diagnosed with acalculous gangrenous cholecystitis during the recovery period after the COVID-19 infection in Italy, and the patients were discharged without any problem.

It is noteworthy that in our study population, the duration of hospital stays of the patient group undergoing PC prolonged. The average PC insertion time was 3.54 days, which is similar to the data reported in the literature. Clinical recovery time after PC was also similar to the literature, but the time from initial presentation to discharge was longer.

In the present study, we observed that the PC group had higher CRP and WBC levels at the time of emergency admission, and the dimensions and wall thickness of the gallbladder increased in imaging tests of this patient group. We also think that the patients in the PC group were older and had more additional diseases compared to the other two groups. Although there were significant differences in the initial clinical presentations of these patients, we think that the delay in PC insertion is reflected in the length of hospital stay. However, the fact that one of the patients that were examined in the emergency room and treated and followed up at the outpatient department needed hospitalization may be considered as an achievement.

The limitations of the present study include the retrospective design, the low number of patients, the absence of PCR testing for COVID-19 for some patients, the lack of standardization in imaging tests, and also subjective findings, such as physical examination results, that were recorded by different people.

We think that using non-surgical treatment methods effectively in all patients with AC who apply to the emergency room during the pandemic, we were able to protect both the patients and the health personnel in terms of coronavirus infection in our hospital located in Istanbul, the epicenter of the pandemic in Turkey.

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ORJİNAL ÇALIŞMA - ÖZET

COVID-19 pandemisi süresince acil servise başvuran akut kolesistit hastalarına genel yaklaşımımız ve perkütan kolesistostomi deneyimi

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GEREÇ VE YÖNTEM: 11 Mart 2020 ile 31 Mayıs 2020 tarihleri arasında hastanemiz acil servisine AC nedeniyle başvuran 72 hasta çalışmaya dahil edildi. Hastalar ayaktan tedavi edilen (Grup 1), yatırılarak tedavi edilen (Grup 2) ve perkütan kolesistostomi ile tedavi edilen (Grup 3) olmak üzere üç gruba ayrıldı. Bu üç gruba demografik ve klinik özellikleri karşılaştırıldı.

BULGULAR: Grup 1'de 36 (%50), Grup 2'de 25 (%34,7) ve Grup 3'te 11 hasta (%15.3) vardı. Hastaların demografik özellikleri birbirine benzerdi. Grup 3'teki hastaların acil servise başvuru anındaki CRP ve WBC değerleri diğer iki gruba göre yüksekti. Ayrıca Grup 3'teki hastalarda safra kesesi duvarı daha kalın, kese boyutu daha büyük saptandı. Hastaların ortanca 3.5 günde perkütan kolesistostomi takılığı ve yatış gününün Grup 2'deki hastalara kıyasla daha uzun olduğu saptadık (sırasıyla, 3.9 gün ve 9.2 gün, p=0.00). Taburculuk sonrası yeniden yatış oranları birbirine close daylandığı belirtildi. Ayaktan takip yapılan Grup 1'deki hastaların tamamında cerrahi gerektiren acil bir durum ortaya çıkmadı ve mortalite izlenmedi. Yetmiş iki hastanın tamamında cerrahi gerektiren acil bir durum ortaya çıkmadı ve mortalite izlenmedi.


Anahtar sözcükler: Akut kolesistit; COVID-19; perkütan kolesistostomi.