COVID-19 Outbreak and Acute Cholecystitis in a Hub Hospital in Milan: Wider Indications for Percutaneous Cholecystostomy.

Matteo Barabino
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Gaetano Piccolo
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Arianna Trizzino
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Veronica Fedele
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Carlo Ferrari (carlo.ferrari1@unimi.it)
Università degli Studi di Milano https://orcid.org/0000-0001-5118-2340
Vincenzo Nicastro
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Andrea Pisani Ceretti
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Enrico De Nicola
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Nicolò Maria Mariani
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Marco Giovenzana
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Giovanna Scifo
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Massimiliano Mazza
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Ruggero Vercelli
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Roberto Santambrogio
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Carmelo Luigiano
Universita degli Studi di Milano Facolta di Medicina e Chirurgia
Enrico Opocher

Universita degli Studi di Milano Facolta di Medicina e Chirurgia

Research article

Keywords: acute cholecystitis, percutaneous cholecystostomy, COVID-19, SARS-CoV-2, bedside, drainage

Posted Date: September 24th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-69267/v1

Version of Record: A version of this preprint was published at BMC Surgery on April 6th, 2021. See the published version at https://doi.org/10.1186/s12893-021-01137-y.

Abstract

BACKGROUND.

COVID-19 pandemic has impacted the Italian national health care system at many different levels, causing a complete reorganization of surgical wards. In this context, in this study we retrospectively analyzed our management strategy for patients with acute cholecystitis.

METHODS.

We analyzed all patients admitted to our Emergency Department for acute cholecystitis from February 27th to April 30th, 2020. We graded each case according to the 2018 Tokyo Guidelines. All patients were tested for positivity to SARS-CoV-2 and received an initial conservative treatment.

RESULTS.

Thirty-seven patients were admitted for acute cholecystitis (13 grade I, 16 grade II and 8 grade III). According to Tokyo Guidelines 2018, patients were successfully treated with antibiotic only, bedside percutaneous transhepatic gallbladder drainage and laparoscopic cholecystectomy in 29.7%, 21.6 % and 48.7% of cases respectively. Therapeutic strategy of three out of 8 cases, otherwise fit for surgery, submitted to percutaneous transhepatic gallbladder drainage (37.5%), were directly modified by COVID-19 pandemic: one due to the SARS-CoV-2 positivity, while two others due to unavailability of operating room and intensive care unit for post-operative monitoring respectively. Overall success rate of percutaneous drainage was of 87.5%, the mean post-procedural hospitalization length was 9 days, and no related adverse event were observed.

CONCLUSIONS.

Bedside cholecystostomy has shown to be an effective and safe treatment, which acquired an increased relevance in the present acute phase of the pandemic. This strategy will potentially be taken into consideration in future phases, when the coexistence with the virus will require us to respond in an even more virtuous fashion.

Background

COVID-19 is a respiratory tract infection caused by the new SARS-CoV-2 virus, firstly recognized in December 2019 in Wuhan city, Hubei, China.

Worldwide, almost 3 million cases are counted with a total of 216.000 deaths(1). In Italy, the first case has been notified in Codogno (Lodi, Lombardy) on the 21st of February(2).

Most infected people only develop a mild illness, while about 14% of cases evolve into severe respiratory syndrome that requires hospitalization. Among these cases, about 5% of people need admission to intensive care units (ICU) with a mean length of hospital stay of 15 days(3).

After that, the infection rapidly spread in Italy: we are currently counting a total of 201.505 infected cases, 27.359 deaths and 68.941 recovered. Lombardy is the most hit region with 74.348 people positive to COVID-19, of which 18.837 only in Milan(4).

Our University Hospital is a Covid-19 Hub and the Emergency Department has been re-adapted in order to face the pandemic emergency.

The majority of resources were allocated for the symptomatic patients' care in the Emergency Room (ER). Surgical Departments were completely reorganized: urgent and oncologic cases of all branches (General, Vascular, Otolaryngology, Maxillofacial Surgery, Urology and Thoracic Surgery) were incorporated in one single surgical ward.

In the last two months (from March to April), we experienced a decrease in accesses to Emergency Room for surgical acute diseases, due to quarantine status and fear of infection. Many people with acute appendicitis, diverticulitis or cholecystitis were treated at home, following instructions given by General Practitioners.

Among patients admitted to the ER for gallbladder stones-related diseases, we observed a higher rate of severe acute cholecystitis, often characterized by prolonged and under-treated symptomatology.

In this study we retrospectively analyzed our management strategy and how it has been influenced by COVID-19 pandemic.

Methods

We retrieved medical records of all patients admitted to our Emergency Department for Acute Cholecystitis (AC) from February 27th to April 30th, 2020. We graded the severity of each AC according to the Tokyo 2018 (TG-18) score(5). The American Society of Anesthesiologists score (ASA) and the Charlson Comorbidity Index (CCI) were adopted to evaluate the surgical risk(6, 7).

We also estimated the SARS-CoV-2 infection risk by administering a questionnaire regarding COVID-19 symptomatology and possible contacts with infected cases. Moreover, all patients were tested for positivity to SARS-CoV-2 by means of a nasopharyngeal swab.

With regards to the standard indications provided by the Tokyo guidelines, we introduced, due to force majeure, COVID as a variable (Fig. 1): in case of positivity to SARS-CoV-2, patients were admitted to COVID-dedicated wards and they were treated conservatively (antibiotic versus bedside percutaneous drainage). In case of negative nasopharyngeal swabs, given the limited availability of operating theatres and medical and nursing staff employed in the intensive care units saturated with COVID patients, we adopted, whenever possible, a conservative strategy, thus reserving surgery for selected patients only. This approach was in line with our national surgical protocols and with the American College of Surgeons and the Royal College COVID-19 guidelines(8, 9). When antibiotic therapy failed, if the operating theatre and a bed in the intensive care unit were available, cholecystectomy was recommended, according to the TG-18 guidelines(5). We adopted a standard laparoscopic approach and, in order to limit any possible spread of the virus due to nebulization during laparoscopy, the surgical team was provided with adequate personal protective equipment (FFP2 masks and visors). We also implemented a specific filtration system for a safe carbon dioxide evacuation at the end of the laparoscopic procedure. The filtration system is composed of a small rubber tube connecting the gas outlet of one of the trocars to a filter usually mounted on mechanical ventilation machines (Minz's device)(10). Lastly, patients showing no benefits from antibiotic treatment, but considered "not fit" for surgery received a bedside percutaneous trans-hepatic gallbladder drainage (PTGBD).

Results

Overall results

During the COVID-19 pandemic, we observed 37 patients admitted to Emergency Room for AC. The mean age of our patients was 64 (range: 38–94 yo) with a slight male prevalence (56.7%). Patients were stratified according to the Tokyo Guidelines 2018: 13 grade I, 16 grade II and 8 grade III. The remaining demographic, clinical and perioperative characteristics of our population are summarized in Table 1.

Table 1
Demographic, Clinical and Operative Data of Patients

Age (yo - mean and range)	**64**	**(38–94)**
Sex (%)		
Male	21	(56.7%)
Female	16	(43.3%)
BMI[a] (mean ± SD)	26. 5	(± 3.9)
ASA[b] score (%)		
1–2	27	(72.9%)
3–4	10	(27.1%)
CCI[c] (%)		
< 6	32	(86.5%)
≥ 6	5	(13.5%)
Severity grade according to 2018 Tokyo Guidelines (%)		
Grade I	13	(35.1%)
Grade II	16	(43.3%)
Grade III	8	(21.6%)
Treatment (%)		
Antibiotics only	11	(29.7%)
PTGBD[d]	8	(21.6%)
Lap-C[e]	18	(48.6%)

[a] Body Mass Index; [b] American Society of Anesthesiology; [c] Charlson Comorbidity Index; [d] Percutaneous transhepatic gallbladder drainage; [e] Laparsocopic cholecystectomy.

One patient resulted SARS-CoV-2 positive and was admitted to the Internal Medicine COVID ward where he was treated conservatively (antibiotics, fluid resuscitation and bowel rest). Three days after the beginning of antibiotic therapy, the patient developed early clinical features of sepsis and underwent an emergency bedside PTGBD. This procedure improved the clinical picture and the patient was discharged from the hospital on the tenth day after the nasopharyngeal swab test negativitization.

In SARS-CoV-2 negative patients, a complete resolution of AC was achieved with only antibiotic therapy in 11 out of 36 cases (30.5%). Eighteen patients (50%) with a low surgical risk (ASA 1–2, CCI < 6 and < 75 yo) underwent laparoscopic cholecystectomy following the initial antibiotic therapy. Among SARS-CoV-2 negative patients, a bedside PTGBD was performed in 7 cases (19.4%), of which 1 patient grade I, 3 grade II and 3 grade III, according to TG-18 AC severity grading. Success rate of PTGBD was of 87.5% and the mean post-procedural hospitalization length was 9 days (SD ± 3 days). Only one patient required emergency laparoscopic cholecystectomy (Lap-C), due to a persistent septic status 5 days after positioning of the percutaneous drainage. The following post-operative course was regular and the patient was discharged on the third post-operative day. The PTGBD procedures were not aggravated by any complication. The allocation of different approaches according to AC severity is summarized in Table 2.

Table 2
Therapeutic approaches according to severity grades (TG-18a)

	GRADE I	GRADE II	GRADE III
Antibiotics only	0	7 (43.7%)	4 (50%)
PTGBD[b]	2 (15.4%)	3 (18.7%)	3 (37.5%)
Cholecystectomy	11 (84.6%)	6 (37.6%)	1 (12.5%)

[a] 2018 Tokyo Guidelines; [b] Percutaneous transhepatic gallbladder drainage

Results according to TG-18 severity grading

Grade I. Almost all patients (11/13) were considered fit for surgery (ASA1-2, CCI < 6 and age < 75 yo) and were admitted to the Emergency Room (ER) within the optimal timeframe (symptoms onset < 72 h) to be managed by early Lap-C. We did not experience any conversion to laparotomy. Two patients developed post-operative jaundice due to residual common bile duct stones requiring ERCP. One patient had post-operative fever due to a 15 mm fluid collection in the gallbladder bed, successfully treated with antibiotics. In all these cases, the remaining postoperative course was uneventful and all patients recovered successfully. The mean hospital stay was 5 days (range 2–12).

Two cases were treated with PTGBD. One patient with high surgical risk (ASA 3, CCI 6, 88 y o) did not respond to broad spectrum antibiotics and received a bedside PTGBD. The second case is represented by a 58 years-old man, fit for surgery, but SARS-Cov2 positive: therefore, the patient received upfront PTGBD (Fig. 2).

Grade II. Out of 16 patients, 7 showed a resolution of the clinical picture by means of antibiotic therapy alone. In seven patients with low surgical risk (ASA 1–2, CCI < 6 and age < 75 y o), early Lap-C was indicated: of these, one patient could not be operated due to operating room staff unavailability caused by the COVID emergency. This patient was treated with percutaneous drainage. Two patients did not respond to antibiotic and were also considered not fit for surgery (ASA 3, CCI > 6 and age > 75 y o); therefore, they underwent bedside PTGBD (Fig. 3).

Grade III. Fifty percent (4/8) of cases showed a resolution of the clinical picture with conservative treatment alone. A young patient with low surgical risk (ASA 1, CCI 0) underwent surgical treatment due to lack of response to antibiotic therapy. Three patients underwent a bedside PTGB: two elderly patients with many comorbidities (ASA > 3, CCI > 4) and a young, asthmatic female that would have required post-operative ICU monitoring. (Fig. 4).

Discussion

The optimal treatment for acute, stone-related cholecystitis is considered antibiotic therapy followed by early cholecystectomy(5–11). In selected cases, when surgery is not feasible due to concomitant sepsis, severe comorbidities, poor performance status or bad timing (> 72 h from the onset of symptoms), the treatment of choice is represented by a conservative strategy consisting of antibiotic therapy, with success rate of 76% and recurrence of symptoms of 18%(11). When antibiotic therapy alone is unsuccessful, PTGBD is considered a safe and valid therapeutic option as a temporary and sometimes definitive alternative to surgery, especially in elderly patients (> 80 y o) with high surgical risk (12–14).

In the present COVID era, this conservative approach has regained its relevance in our country, especially in Milan, which is one of the most affected districts. Indeed, the conservative strategy mentioned above fits into a context of resource optimization and review of surgical indications, since almost 90% of our operating theatres were used for the treatment of COVID ventilated patient. In our present series we successfully treated 51.3% of patients affected by AC conservatively. In particular, 29.7% of cases were treated through antibiotic therapy alone and 37.5% of patients were treated through PTGBD. The latter represents a significantly increased percentage as compared to the rate of PTGBD interventions performed in the non-COVID era (9%) found in the literature (15). There are several possible reasons explaining the increased number of PTGBD interventions performed. First, the use of PTGBD is related to a delayed diagnosis of the disease in patients fearing to visit hospital facilities at the early stage of the pandemic. Second, the reduced availability of hospital beds and medical/nursing staff resources, actively tackling the treatment of COVID patients, forced physicians to apply a more conservative approach to patient management.

In line with the hypothesis that patients presented themselves with significant delay at the ER for a clinical evaluation, we observed that only 13 patients had grade I AC according to TG-18, while the remaining 24 patients had a more aggressive and advanced disease manifestation (grade II or III).

We approached each patient according to the Tokyo guidelines.

Table 2 shows how surgical approach was the treatment of choice for grade I patients (Lap-C 84.6%vs PTGBD 15.4%); on the other hand, increasing grade and disease severity mirrored a more conservative strategy (grade III: Lap-C 12.5%vs antibiotic +/- PTGBD 87.5%). The COVID-19 pandemic forced us to adopt a more conservative approach with respect to what has been established in the Tokyo guidelines. In particular, 3 out of 8 patients submitted to PTGBD (37.5%) would have been optimal candidates for Lap-C in a non-COVID era. One grade I patient, theoretically fit for surgery, turned out to be SARS-CoV-2 positive; therefore, he underwent PTGBD for two main reasons. First, the percutaneous approach represented a less invasive, yet valid alternative to a more labored surgical management in a SARS-CoV-2 positive patient. Moreover, data from a Chinese report, seem to highlight how surgical stress in SARS-CoV-2 positive patients may promote and accelerate the respiratory disease, with a subsequent increased post-operative mortality rate(16). For these reasons and according to the international scientific community consensus, we pursued the idea of implementing non-operative management for acute cholecystitis whenever possible(9).

In one patient with a grade II AC, Lap-C was precluded due to the unavailability of operating room staff, which was engaged in the management of COVID-19 patients. Moreover, we had to exclude from Lap-C a 37 years old woman with grade III AC, due to severe asthma. In fact, being at higher risk of post-operative respiratory failure, the patient would have needed post-operative ICU monitoring at a time when beds were not available because fully occupied by COVID-19 ventilated patients.

Other reasons to rely on PTGBD are represented by its efficacy, safety and reproducibility at the patient's bedside. The major advantage of this approach was to release additional workload from the operating room staff, which was almost totally deployed to deal with COVID patients. Our analysis showed that PTGBC did not influence the average length of stay of our patients. This result may be related to two main reasons. First, our outcome is severely affected by outliers, such as duration of hospitalization of the only SARS-CoV-2 positive patient in this series. The post-procedural course was uneventful, with fast recovery from symptoms related to AC. However, the patient had to wait the negativization of the nasopharyngeal swab before being discharged home, thus increasing the length of hospital stay. Moreover, the mean length of stay was affected by severe delay in the transfer of elderly patients to nursing homes or rehabilitation facilities after the resolution of AC. In fact, also these structures have been severely impaired in their receptive ability due to the pandemic side-effects.

When the procedure is performed within the first 24 hours following the onset of symptoms, PTGBD is related to short hospital stay and low complication rate (0.5%), such as bleeding(5). International literature describes a drainage occlusion rate of 10% and a dislocation in 15% of cases(17), while success rate is 85% (characterized by complete clinical remission and infection resolution)(18). In our experience, we performed cholecystostomy in all patients within 72 hours from the onset of clinical signs and we did not observe any peri-procedural complication. In 87.5% of cases we obtained complete regression of symptoms after percutaneous drainage within 24 hours; only one patient underwent urgent Lap-C due to a persistent septic status 5 days after PTGBD. Eventually, it is essential to highlight how the bedside approach we adopted for percutaneous drainage allowed the reduction of unnecessary transfers of patients to the radiology department, thus minimizing the risk of virus spread.

Conclusions

Our data demonstrates how the number of performed percutaneous cholecystostomies increased since the beginning of the pandemic. The COVID-19 pandemic discouraged patients from seeking clinical evaluation due to increased fear of attending hospital facilities. Also, the pandemic changed the physicians' attitudes, who opted for solutions with a lower clinical impact in order to dedicate the majority of their resources to achieve their main objective: the management and treatment of COVID patients. Bedside cholecystostomy has shown to be an effective and safe treatment, which acquired an increased relevance in the present acute phase of the pandemic. This strategy will potentially be taken into consideration in future phases, when the coexistence with the virus will require us to respond in an even more virtuous fashion.

Appendix - List Of Abbreviations

AC: acute cholecystitis

ASA: American Society of Anesthesiologists

CCI: Charlson Comorbidity Index

ER: emergency room

ICU: intensive care unit

Lap-C: laparoscopic cholecystectomy

PTGBD: percutaneous transhepatic gallbladder drainage

SD: standard deviation

TG-18: 2018 Tokyo guidelines

Declarations

- **Ethics approval and consent to participate**: all procedures performed in the study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Because of the retrospective nature of this study, any ethical committee approval was deemed unnecessary according to national regulations.

As our manuscript appears to report data on patients with COVID-19, we confirm that these patients have not been reported in any other submission by you or anyone else.

- **Consent for publication:** not applicable.
- **Availability of data and materials**: the dataset used during the current study are available at https://www.synapse.org/#!Synapse:syn22162934/files/
- **Competing interests**: the authors declare that they have no competing interests.

- **Funding**: authors did not receive any funding for this publication.

- **Authors' contribution**: all authors have read and approved the manuscript.
    - Conceptualization of the study: BM.
    - Investigation: BM, PG.
    - Data analysis: TA, FV, FC, NV.
    - Supervision: OE, SR, PCA, DNE, VR.
    - Writing original draft: BM, PG, FC.
    - Review the article: MM, MNM, SG, GM, LC, VR.

- **Acknowledgements**: not applicable

References

1. Ryu S, Chun BC. Epidemiological characteristics of 2019 novel coronavirus: an interim review. Epidemiol Health. 2020;
2. Gagliano A, Villani PG, Cò FM, Paglia S, Bisagni PAG, Perotti GM, et al. 2019-ncov's epidemic in middle province of northern Italy: Impact, logistic & strategy in the first line hospital. Disaster Med Public Health Prep. 2020;1–5.
3. World Health Organization. Clinical management of when novel coronavirus is suspected: severe acute respiratory infections What to do and what not to do. WHO. 2020;
4. Ministero della Salute: Covid-19 - Situazione in Italia. [Internet]. Available from: www.salute.gov.it.
5. Okamoto K, Suzuki K, Takada T, Strasberg SM, Asbun HJ, Endo I, et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. J Hepatobiliary Pancreat Sci. 2018;
6. Delegates ASA House of. American Society of Anesthesiologists classification. In: ASA Relative Value Guide. 2014.
7. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis. 1987;
8. The American College of Surgeons ACS COVID-19 and Surgery [Internet]. 2020. Available from: www.facs.org/covid-19/clinical-guidance
9. The Royal College of Surgeons Updated Intercollegiate General Surgery Guidance on COVID-19 [Internet]. 2020. Available from: www.rcseng.ac.uk/coronavirus/jointguidance-for-surgeons-v2

10. Mintz Y, Arezzo A, Boni L, Chand M, Brodie R, Fingerhut A. A Low Cost, Safe and Effective Method for Smoke Evacuation in Laparoscopic Surgery for Suspected Coronavirus Patients. Ann Surg. 2020;
11. Ansaloni L, Pisano M, Coccolini F, Peitzmann AB, Fingerhut A, Catena F, et al. 2016 WSES guidelines on acute calculous cholecystitis. World Journal of Emergency Surgery. 2016.
12. Peitzman AB, Watson GA, Marsh JW. Acute cholecystitis: When to operate and how to do it safely. J Trauma Acute Care Surg. 2015;
13. Gutt CN, Encke J, Köninger J, Harnoss JC, Weigand K, Kipfmüller K, et al. Acute cholecystitis: Early versus delayed cholecystectomy, a multicenter randomized trial (ACDC Study, NCT00447304). In: Annals of Surgery. 2013.
14. Mariani N, Pisani Ceretti A, Fedele V et al. Surgical strategy during the COVID-19 pandemic in an University metropolitan Hospital in Milan, Italy. World J Surg. 2020;([Ahead of print]).
15. Er S, Berkem H, Özden S, Birben B, Çetinkaya E, Tez M, et al. Clinical course of percutaneous cholecystostomies: A crosssectional study. World J Clin Cases. 2020;
16. Lei S, Jiang F, Su W, Chen C, Chen J, Mei W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. EClinicalMedicine. 2020;
17. Dewhurst C, Kane RA, Ní Mhuircheartaigh J, Brook O, Sun M, Siewert B. Complication rate of ultrasound-guided percutaneous cholecystostomy in patients with coagulopathy. Am J Roentgenol. 2012;
18. Ito K, Fujita N, Noda Y, Kobayashi G, Kimura K, Sugawara T, et al. Percutaneous cholecystostomy versus gallbladder aspiration for acute cholecystitis: A prospective randomized controlled trial. Am J Roentgenol. 2004;

Figures

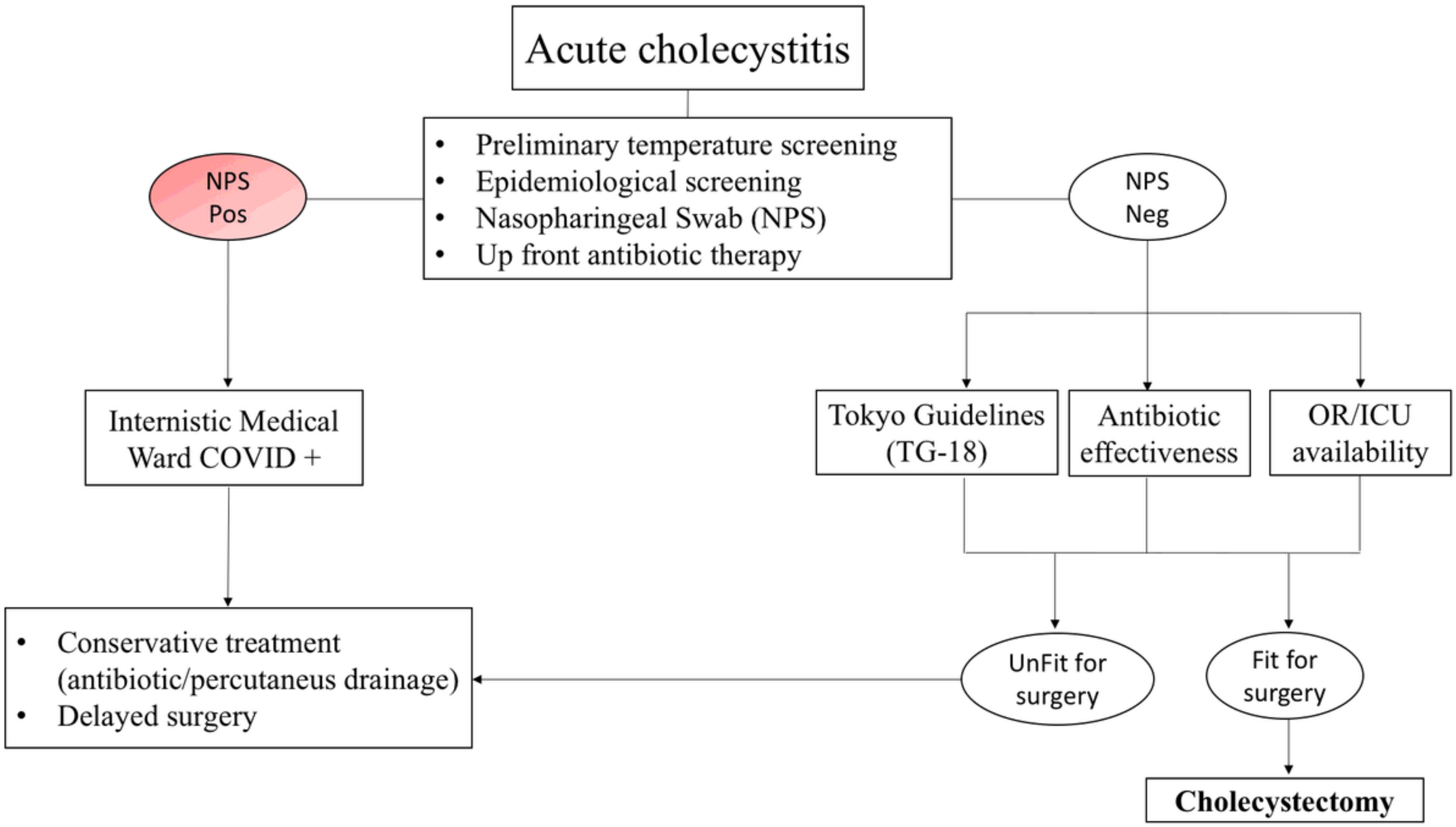

Figure 1

Flow chart of the patients affected by acute cholecystitis during the outbreak period of COVID-19 infection (NPS: nasopharyngeal Swab; TG-18: Tokyo guidelines 2018; OR: operative room; ICU: intensive care unit).

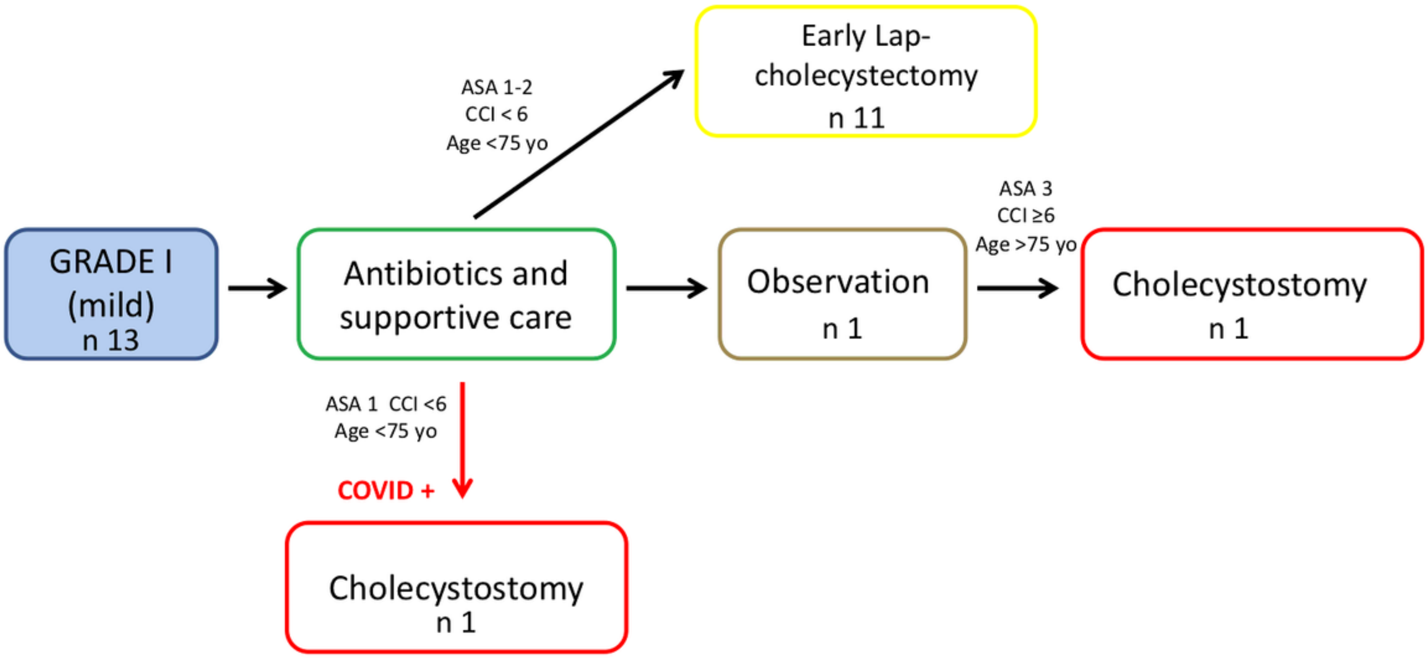

Figure 2

Treatment strategy in Grade I acute cholecystitis.

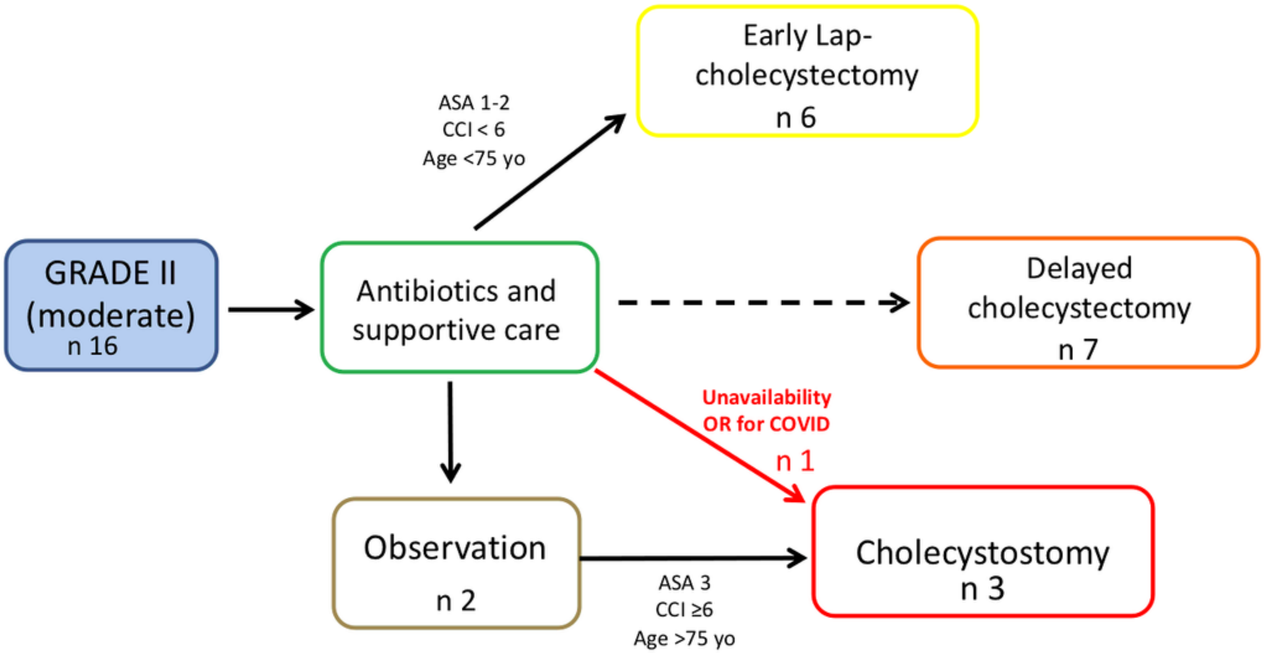

Figure 3

Treatment strategy in Grade II acute cholecystitis.

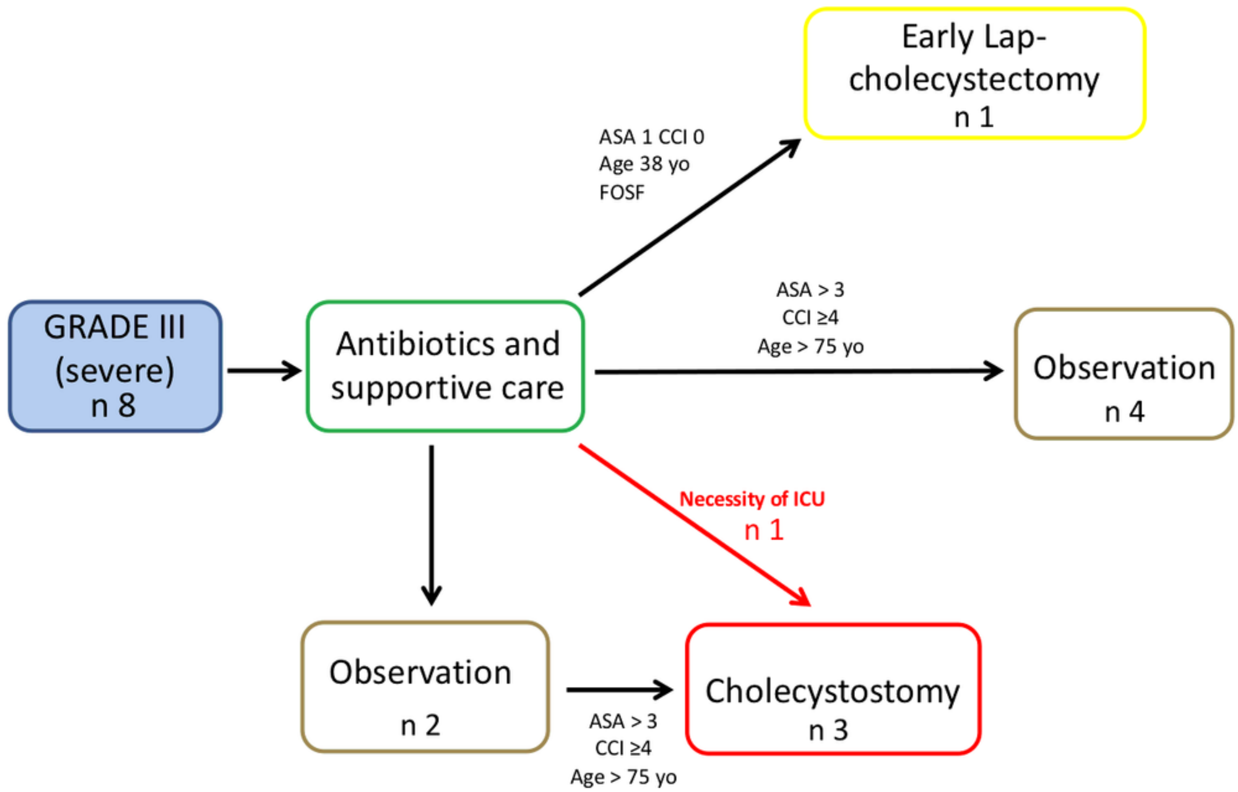

Figure 4

Treatment strategy in Grade III acute cholecystitis.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- DATABASE.xlsx