CHAPTER 3

ACUTE CHOLECYSTITIS TREATMENT

Ahmet Tarık HARMANTEPE[1]

INTRODUCTION

It is estimated that the incidence of gallstones in adults ranges from 10% to 15% (1). The formation of stones in patients can be attributed to various independent factors such as their family background, inherent tendency, cultural heritage, being female, and advancing age (2). Approximately 80-90% of the stones analyzed after removal of the gallbladder are made of cholesterol. The majority, about 80%, of gallstones do not produce symptoms (3). Gallstones can cause blockages in the cystic duct, leading to an enlarged gallbladder and eventually AC, a condition characterized by infection, inflammation, and ischemia. Each year, 1-4% of patients experience biliary colic. Although most gallstones do not cause symptoms, about 25% can result in symptomatic conditions such as cholecystitis, cholangitis, or biliary pancreatitis. Women under the age of 50 are three times more likely to develop AC than men (3).

The standard treatment for AC is LC. It has replaced open surgery because it has less morbidity, less hospital stay, and higher postoperative patient comfort (4,5).

A 2-year prospective multicenter study in Belgium revealed that open surgical and LC approaches were used in 6.8% and 93.2% of patients, respectively. (6). The research discovered that some factors increased the probability of having open surgery, including being over 70 years old, a history of surgery in the upper abdominal area, gangrenous cholecystitis, and being operated on by a surgeon with over 10 years of experience. The conversion rate from laparoscopic to open surgery was 11.4%. Injuries to the bile duct happened in 2.7% of the open surgery patients and 1.1% of the laparoscopic surgery group. Damage to the biliary tract was observed in 13.7% of the cases where open surgery was converted from laparoscopic.

In the study of Teixeira et al., which included 520 patients with cholecystectomy, they found better results in LC compared to open surgery in terms of mortality, preoperative and postoperative surgical complications, and hospital stay (7).

[1] Dr. General Surgeon, Akcakale State Hospital, General Surgery Clinic, tarikharmantepe@gmail.com

DIAGNOSIS

According to the World Society of Emergency Surgery 2020 (WSES) guidelines, the key factors for diagnosing AC are (8):

Clinical history and examination: right upper quadrant tenderness or pain, fever, food intolerance or vomiting, Murphy's sign

Lab tests: high C-reactive protein, high white blood cell count

Radiology: signs of gallbladder inflammation

Clinical examination or laboratory tests alone are insufficient in the 2020 WSES guideline. The first radiological diagnosis method to be chosen after the combination of these two is abdominal ultrasonography (USG), considering its cost-effectiveness. Depending on experience and availability, advanced imaging modalities are recommended. The hepatobiliary iminodiacetic acid (HIDA) scan is more accurate for diagnosing AC compared to other imaging techniques due to its higher specificity and sensitivity. Diagnostic accuracy of computed tomography (CT) is poor. Magnetic resonance imaging (MRI) is as accurate as abdominal ultrasound. A study that only considered patients with a diagnosis of AC compared the diagnostic sensitivities of USG, computer tomography (CT), and HIDA scanning. (9). Their sensitivities were 84.2% for HIDA, 67.3% for USG and 59.8% for CT ($p = 0.017$). HIDA had a clear superiority over CT and USG. No difference was found when CT and US were compared ($p = 0.09$).

TIME FOR SURGICAL INTERVENTION

The timing for surgical intervention for acute cholecystitis is a widely debated topic in the literature. There are studies that have evaluated the benefits of performing an early cholecystectomy (10–12). Early findings suggested that laparoscopic cholecystectomy led to higher rates of conversion to open surgery, prolonged surgical duration, and increased incidence of complications. (13). The timing of surgery for acute cholecystitis has been a topic of debate in the medical community. In the past, early (LC) was considered to result in higher rates of conversion to open surgery, longer operative times, and more complications compared to open surgery. However, with the improvement of laparoscopic techniques, early LC has now become the standard treatment for AC. Studies have shown that there is no significant difference in terms of mortality, morbidity, and duration between early LC and open surgery. The appropriate timing for cholecystectomy is still being discussed in the medical literature (10,12). Studies evaluating the value of AC early cholecystectomy are available (12,14). Recent data have shown that agreeing on a strategy to support early LC provides significant cost savings over different

healthcare systems (15–17). It is not surprising that the included studies were highly biased and thus resulted in very low levels of evidence. However, it was concluded that early LC in the patient with acute cholecystitis is safe and shortens the hospital stay (18,19). However, there is no common agreement on what time period the term 'early' covers for the surgical management of AC. Nevertheless, 'early surgery' is associated with fewer conversions, lower morbidity, and shorter hospital stays. (19,20). Consequently, a 72-hour timeframe for surgery in cases of acute cholecystitis has become the accepted practice. To date, only one well-designed prospective randomized trial has been conducted to address the lack of evidence for the surgical management of AC. (16). "Acute Cholecystitis: The Early vs. Delayed Cholecystectomy" study convincingly demonstrated that emergency cholecystectomy is within 24 hours of admission (21). After conservative antibiotic therapy, the early LC cohort significantly reduced operative time and hospital stay compared to the early LC (<72 hours post-admission) group and the delayed LC (>6 weeks post-admission) group (19). The rate of conversion and entire complication weren't significantly different for the two groups (19,22). It was also stated that 9.7%-23% of AC patients treated non-surgically went to emergency LC (22,23). Roulin et al. stated that similar when comparing LC administered to groups with symptoms before and after 72 hours (24).

In conclusion, LC should be performed within 72 hours of admission in patients with acute cholecystitis (AC). This is in accordance with the recommendations of the Tokyo Guidelines of 2013 and 2018, which suggest that LC should be performed promptly, within 72 hours of symptom onset and after admission. (25,26). Recent studies show that LC performed for patients with symptom onset greater than 72 hours has better outcomes compared to 4-6 weeks delayed LC.

PERCUTAN CHOLECYSTOSTOMY (PC)

In patients with high comorbidity, postoperative mortality in LC is estimated to be 5-30% (27). For these patients, PC was an alternative, which reduced mortality (27). Moderate evidence is recommended in the WSES 2020 guideline for patients at risk for surgery but not responding to medical therapy (8). A study published in 2016 comparing PC and cholecystectomy in critically ill patients reported no benefit from PC use over cholecystectomy (28). Six studies were analyzed with a total of 337,500 patients. Length of hospital stay, mortality, and the quantity of repeat hospital admissions for illnesses connected to gallstones was notably greater in the PC group compared to the group who underwent cholecystectomy. However, the studies were retrospective and their results were biased. The first randomized study on this topic was published. Results showed that laparoscopic

cholecystectomy was superior to PC (29). Abi-Haidar et al. showed that, compared with cholecystectomy (open and laparoscopic), PC is associated with significantly longer ICU length of stay, longer hospital stay, more complications, and higher readmission rates (30). PC and surgical cohorts had comparable mean body temperatures, time to diagnosis after symptom onset, time to antibiotic onset, and AC severity. However, compared to the cholecystectomy group, PC patients were older and had higher WBC counts, alkaline phosphatase levels, American Society of Anesthesiologists classes, and Charlson comorbidity index scores. These factors cause the bias of the study. Patients in the intensive care unit (ICU) with similar preoperative characteristics experienced a slight increase in mortality rate and a significantly higher morbidity rate when undergoing planned cholecystectomy (PC) or emergency cholecystectomy. The morbidity rate was 8.7% after PC and 47% after the surgery. (31).

Although there is conflicting data regarding the reasons for PC, there is consensus that the decision to proceed with PC should be made promptly, within less than 24 hours after the onset of symptoms, if it is to be made at all. Early PC has been shown to reduce hospital stay and procedure-related bleeding in patients with severe AC who are not suitable for surgery, compared to PC performed after 24 hours.(32).

The ideal time for gallbladder removal after PC is a matter of debate. A study that compared early surgery (within 72 hours) to delayed surgery (more than 72 hours) after PC found a higher incidence of postoperative complications and a longer duration of the procedure for the early surgery group, but shorter hospital stays for patients who received early surgery. (33). Another study found that early surgery (within 72 hours) after planned cholecystectomy (PC) had a higher incidence of bleeding and longer surgical time compared to delayed surgery (more than 5 days).(34). Another report stated that there was no difference between early surgery (within 10 days) and delayed surgery (more than 10 days) in terms of the rates of complications, surgical duration, conversion rates, and total hospital stay (35). More prospective studies are needed.

ENDOSCOPIC INTERVENTION

The gold standard in AC is LC. However, there are methods that can bridge the postponed surgical intervention for some high-risk patients or that can be the last treatment for some high-risk patients with surgery. These are PC and endoscopic methods. These endoscopic procedures are transpapillary naso-gallbladder drainage tube (ENGBD), endoscopic transpapillary gallbladder drainage (ETGBD), or transmural ultrasonography-guided gallbladder drainage (EUS-GBD).

In a randomized controlled study by Itoi et al. involving 73 consecutive patients with AC, overall technical success rates of 91.9% and 86.1% were achieved with ENGBD and EGBS, respectively, while treatment success rates were 86.5% and 77.8%. The authors claimed that the lower rate of successful treatment was due to insufficient gallbladder drainage and blockage of small-sized catheters or stents when there are large stones or abscesses present. (36).

A study that compared endoscopic ultrasound-guided gallbladder drainage (EUS-GBD) and PC found similar technical success rates for both methods (97% for EUS-GBD vs 97% for PC, p=0.001), similar clinical success rates (100% for EUS-GBD vs 96% for PC, p=0.0001), and similar rates of complications (7% for EUS-GBD vs 1% for PC, p=0.492), indicating that EUS-GBD is a safe alternative to PC for patients who are not suitable for surgery. (37)

Irani et al. arrived at comparable conclusions based on a retrospective study conducted at multiple centers. In this study, the technical success rates of EUS-GBD and PC were 98% and 100% ($p = 0.88$) respectively. (38) . Furthermore, the group who underwent EUS-GBD had a shorter hospital stay and fewer repeat interventions ($p < 0.05$).

A study with a long-term follow-up of patients after EUS-GBD showed that recurrence of cholecystitis occurred in 7.7% of cases. This suggests that this endoscopic procedure is a secure alternative for treating acute cholecystitis in high-risk patients (39).

EUS-GBD has also proven to be a suitable technique for the conversion of percutaneous cholecystostomy. (40). The advantages of EUS-GBD over PTGBD include the internalization of bile, eliminating the risk of recurrent cholecystitis and bleeding following percutaneous catheter removal, and associated with less post-procedural pain. (40,41).

If carried out by experienced endoscopists, EUS-GBD using self-expandable metal stents (LAMS) to secure the lumen is preferred over ETGBD. Khan et al. recently conducted a meta-analysis and found that the proportional difference of the weighted pooled rates for technical success and clinical success between EUS-GBD and ETGBD was 10% and 4% respectively.(42). This discrepancy is due to the fact that transpapillary procedures can be technically challenging because of the anatomy of the cystic duct or stones. However, if the distance between the gallbladder and the enteric lumen is less than 1 cm, EUS-GBD is safe and feasible (39,41). This method promotes anatomical bile drainage, which results in the creation of a permanent connection (fistula) between the gallbladder and the hollow organs. (43).

The 2020 WSES guideline recommends removing metal stents used in EUS-GBD within 4 weeks to avoid blockage of the lumen and reduce the risk of recurrent AC (8).

ANTIBIOTIC THERAPY

The 2020 WSES guidelines recommend administering antibiotics based on the most commonly found microorganisms, taking into account local antibiotic resistance and drug availability. In biliary infections, the most commonly isolated bacteria are Gram-negative aerobes and anaerobes such as E. coli and K. pneumoniae, as well as B. fragilis (44,45). The role of Enterococci in causing biliary sepsis is uncertain and providing treatment specifically against these microorganisms is not a standard recommendation for biliary tract infections that are acquired in the community. (46). The biggest issue with antibiotic resistance in biliary tract infections is the production of extended-spectrum beta-lactamases by Enterobacteriaceae bacteria. This is commonly seen in patients who have had prior exposure to antibiotics in community-acquired infections. (44,45).

In the study, the authors discovered that postoperative antibiotics did not lower the rate of infectious complications compared to only continuing preoperative antibiotics. This indicates that using postoperative antibiotics as a routine practice may not be necessary for patients undergoing cholecystectomy for uncomplicated acute cholecystitis. (47). The results of the study showed that there was no change in the rate of postoperative infections.

CONCLUSION

The curative treatment of acute cholecystitis is LC or open cholecystectomy. The optimal time for LC is within the first 72 hours from the start of symptoms. For patients who are at high risk and not suitable for surgery, endoscopic or percutaneous gallbladder drainage can be done as a temporary solution until a final treatment or delayed surgery can be performed.

Keywords: acute cholecystitis, treatment, surgical timing, percutaneous cholecystostomy

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