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Acute Cholecystitis

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Keywords

Acute cholecystitis · Surgery · Laparoscopic cholecystectomy · Cholecystotomy · Interdisciplinary management

Summary

Background: The treatment of acute cholecystitis has been controversially discussed in the literature as there are no high-evidence-level data yet for determining the optimal point in time for surgical intervention. So far, the laparoscopic removal of the gallbladder within 72 h has been the most preferred approach in acute cholecystitis. **Methods:** We conducted a systematic review by including randomized trials of early laparoscopic cholecystectomy for acute cholecystitis. **Results:** Based on a few prospective studies and two meta-analyses, there was consent to prefer an early laparoscopic cholecystectomy for patients suffering from acute calculous cholecystitis while the term 'early' has not been consistently defined yet. So far, there is new level 1b evidence brought forth by the so-called 'ACDC' study which has convincingly shown in a prospective randomized setting that immediate laparoscopic cholecystectomy – within a time frame of 24 h after hospital admission – is the smartest approach in ASA I–III patients suffering from acute calculous cholecystitis compared to a more conservative approach with a delayed laparoscopic cholecystectomy after an initial antibiotic treatment in terms of morbidity, length of hospital stay, and overall treatment costs. Concerning critically ill patients suffering from acute calculous or acalculous cholecystitis, there is no consensus in treatment due to missing data in the literature. **Conclusion:** Laparoscopic cholecystectomy for acute cholecystitis within 24 h after hospital admission is a safe procedure and should be the preferred treatment for ASA I–III patients. In critically ill patients, the intervention should be determined by a narrow interdisciplinary consent based on the patient's individual comorbidities.

Introduction

In developed countries, the prevalence of gallstones ranges between 10 and 15% among the adult population while family history, genetic predisposition, ethnic background as well as female sex and the patients' age are independent factors contributing to their development [1, 2]. 1–4% of all patients with known cholelithiasis are suffering from biliary colic each year. Most gallstones remain silent but up to 25% become symptomatic in the form of cholecystitis, cholangitis, or biliary pancreatitis [3, 4]. Once a patient has developed symptoms or complications related to gallstones, surgical therapy remains the gold standard because of a high rate of medical re-admission [5] due to the same symptoms or due to pancreatitis or cholecystitis within a discrete time frame. Furthermore, biliary colic is one of the most common precursors of more and even life-threatening gallstone-related complications [6–8].

Treatment of Acute Cholecystitis

Concerning infectious diseases of the gallbladder, acute cholecystitis is most common. It is triggered by three main mechanisms: i) obstruction of the cystic duct by gallstones, ii) release of lysolecithin, and iii) ascending bacterial infection of the biliary fluid [9, 10]. Recent data have shown that the agreement of a strategy favoring early laparoscopic cholecystectomy results in considerable cost savings according to different health care systems [11–13]. The timing of cholecystectomy in patients with acute cholecystitis has been extensively discussed in the literature. Yet, only few studies assessing the value of early cholecystectomy in acute cholecystitis exist [7, 14–17], which are summarized in only one Cochrane review from 2013 [18] and in two meta-analyses [19, 20]. It is not surprising that the bias of the included studies was high, thus resulting in a very low level of evidence. Nevertheless, all authors similarly concluded that early laparoscopic cholecystectomy during acute cholecystitis 'appeared to be safe and shortened the total hospital stay' [18–20]. However, there is no common consent in how to define the term 'early' in the context of surgical therapy of

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acute cholecystitis. In summary, the evidence of early laparoscopic treatment of acute cholecystitis has been based on only less than 500 patients. In the same line of evidence, primary and secondary endpoints of all studies dealing with this topic have not been clearly defined. Nevertheless, 'early cholecystectomy' is associated with lower conversion rates, lower morbidity, and shorter in-hospital stay [19, 21]. Therefore, a timeframe of 72 h until operation due to acute cholecystitis was an accepted pathway. So far, only one large prospective randomized and well-powered study has been conducted to overcome the lack of evidence in the surgical treatment of acute cholecystitis [12]. Gutt et al. [9] have convincingly shown in their 'ACDC (Acute Cholecystitis: Early versus Delayed Cholecystectomy) study' that immediate cholecystectomy – within a timeframe of 24 h after *admission* for acute cholecystitis – was superior to a more conservative approach including initial antibiotic treatment followed by delayed laparoscopic cholecystectomy within 7–45 days regarding postoperative morbidity, hospital stay, and total hospital costs. In addition, patients randomized to the delayed group had a three times higher morbidity in terms of persistence of their symptoms such as cholecystitis, cholangitis, peritonitis, or abscess. A total of 618 patients were either randomized to immediate cholecystectomy (n = 304) or conservative treatment with moxifloxacine (n = 314) in 35 centers, including only patients with a maximal ASA (American Society of Anesthesiologists) III score. Although well-powered and elaborated, the 'ACDC study' does not provide information on how to treat patients with high morbidity (ASA IV and ASA V). In order to transfer the results of the 'ACDC study' to clinical routine, a clear and rapid diagnosis of acute cholecystitis in an interdisciplinary consent is mandatory to reach the timeframe of 24 h after hospital admission. Based on four clinical symptoms, which are i) positive Murphy's sign, ii) pain in the right upper abdominal quadrant, iii) leukocytosis, and iv) fever, the diagnosis of acute cholecystitis could be easily reached. A positive assessment in combination with sonographic signs of cholecystitis, especially edema or sonographic Murphy's sign, can further increase the sensitivity [22–24]. Nevertheless, not all patients with suspected cholecystitis are directly referred to the surgical ward but to a medical emergency department so that in some cases these patients are not exactly fitting into a timeframe of 24 h after hospital admission and cannot consequently be operated on. Therefore, a close and fast interdisciplinary patient flow is mandatory to achieve the optimal time point in the treatment of patients with acute cholecystitis. In Germany, this algorithm was not established in all surgical departments, as shown in a survey from 2009 in which 65% of these surgical centers reported to respect this timeframe often or very often [25].

While the vast majority of patients with acute calculous cholecystitis can safely undergo surgery by means of early laparoscopic cholecystectomy within 24 h after admission [12], some critically ill patients on the intensive care unit may develop cholecystitis without evidence of gallstones. This may require a completely different treatment because of the patient's poor general condition. Acute acalculous cholecystitis may show similar symptoms as the calculous one [26]; however, it is often masked by the patient's concomitant or primary disease, which can be trauma, major abdominal surgery with peritonitis, or major burn injury. In contrast to acute calculous cholecystitis, there are more frequent complications in terms of abscess, gangrene, perforation, or empyema [26]. It also has to be kept in mind that critically ill patients are more prone to infections with multiresistant bacteria [27, 28]. Therefore, morbidity and mortality rates are high and ranging widely in critically ill patients [29–31]. Although removal of the gallbladder is generally the gold standard in any infectious disease of the gallbladder, there is currently only a low level of evidence concerning a surgical or non-surgical approach to critically ill patients with acute cholecystitis since randomized controlled studies are lacking and some retrospective studies were conducted representing only single-hospital experience [30]. So far, there is no consensus in how to define the 'success' of percutaneous cholecystotomy or cholecystectomy. On the one hand, most studies dealing with this topic have defined success as a decrease of septic symptoms after intervention within a time frame of 48–72 h [30]. On the other hand – and in consequence –, the mortality rate, also strongly biased, is an objectively measurable parameter. As shown in a large population-based survey, cholecystotomy has offered no benefit in the subgroup of the sickest patients suffering from severe septic shock [31]. However, it has been shown by the same group – based on a nationwide inpatient sample – that a higher age and more comorbidity are independently associated with the risk of receiving a cholecystotomy instead of a cholecystectomy. It is not surprising that these patients had a longer hospital stay as well as higher mortality rates [32]. Thus, therapy of acute acalculous cholecystitis is an interdisciplinary challenge, and there is – in contrast to acute cholecystitis – no high level of evidence available on how to treat. Therefore, the treatment decision depends on both the surgeon's attitude and the patient's comorbidities. Considering acute calculous cholecystitis in critically ill patients, the evidence is even scarcer as it is based on only two trials from the pre-ACDC period with a total of 156 patients [33].

Conclusion

In summary, patients suffering from acute cholecystitis due to symptomatic gallstones do benefit from an immediate laparoscopic cholecystectomy within a time frame of 24 h after hospital admission; however, it has to be kept in mind that hospital admission time occasionally does not exactly reflect the onset of symptoms. In critically ill patients, therapy of acute cholecystitis – which is often acalculous – remains an interdisciplinary and individual decision.

Disclosure Statement

J.S. and M.G. have nothing to disclose.

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