



Emergency Hepatobiliary Surgery in Elderly

25

Dario Tartaglia, Federico Coccolini, and Massimo Chiarugi

With the increase in life expectancy, hepatic and biliary diseases have become common problems in the elderly. Most acute presentations can be the effect of infectious, inflammatory (gallstones, cholangitis, hepatic abscess), and traumatic (common bile duct, liver) etiologies [1–3]. Among the elderly, bile duct stones are a common cause of clinical problems, such as acute cholecystitis and acute cholangitis. Because of the increasing prevalence of morbidity that accompanies the aging process, urgent and aggressive treatment is required for elderly patients with severe infectious conditions or with traumatic injuries. Many of the hepatobiliary emergencies present with overlapping symptoms, but treatment options can be different [4] and they may include percutaneous, endoscopic, and surgical procedures.

25.1 Acute Calculous Cholecystitis

Old age (>65 years), by itself, does not represent a contraindication to cholecystectomy for acute calculous cholecystitis [5]. However, increased age is associated with increased comorbidities and a decreased life expectancy. As the concept of frailty is becoming more and more common in surgery, several frailty scores have been recently introduced [6–8]. Frailty scoring systems may help in stratifying the risk for patients requiring surgery. However, a consensus about the superiority of one system over the others has not reached yet. ASA, P-POSSUM, and APACHE II have shown the best correlation with surgical risk, but there is no validated way of stratifying risk in elderly patients, even though age is one of the factors taken into account for the calculation of P-POSSUM and APACHE II score [9]. In order to avoid surgery for

D. Tartaglia · F. Coccolini · M. Chiarugi (✉)
Emergency Surgery and Trauma Center Unit, New Santa Chiara Hospital, University of Pisa,
Pisa, Italy
e-mail: dario.tartaglia@unipi.it; federico.coccolini@unipi.it; massimo.chiarugi@unipi.it

elderly and high-risk patients (often these two groups are mixed together), alternative treatments such as the percutaneous drainage of the gall bladder (cholecystostomy) or, less commonly, the drainage of the gallbladder by retrograde endoscopic procedure, have been developed. The results regarding the drainage of the gallbladder are not conclusive and we have to wait for prospective studies to throw some light on this issue [10, 11]. The laparoscopic approach to acute cholecystitis is safer than the open approach: morbidity and mortality, in the case of laparoscopic procedure, are 10% and 1%, respectively compared to 25% and 2% for the open procedure [9]. On the other hand, aged patients are at increased risk of conversion from laparoscopy to open procedure, and this may produce a worsening impact on the final outcome [12–15]. The current opinion is that elderly patients presenting with acute cholecystitis should be offered a laparoscopic approach unless contraindicated by anesthesiologic reasons or by the presence of a septic shock. Laparoscopic cholecystectomy is safe, feasible, with a low complication rate and it is associated with a shortened hospital stay. Early laparoscopic cholecystectomy should be performed as soon as possible but can be safely and reasonably delayed up to 10 days from the onset of symptoms if comorbidities need to be addressed and managed. However, although the historical rule of 72 h to perform cholecystectomy for acute cholecystitis is no longer mandatory, surgery performed as soon as possible is associated with a better outcome [16–21]. The role of routine intraoperative cholangiography (IOC) has been evaluated in patients undergoing elective cholecystectomy [22]. Eight randomized trials (including 1715 patients) were analyzed in a recent systematic review and the conclusion was that there is no clear evidence to support its routine use [23]. Moreover, there are no randomized studies focusing on the use of intraoperative cholangiography during laparoscopic cholecystectomy for acute cholecystitis. As in younger patients, in the elderly IOC should be performed selectively. When no pre-operative CT scan with contrast or MR cholangiography has been done before surgery for acute cholecystitis, IOC may be pursued if the patient shows elevation of the liver biochemical tests (including ALT, AST, bilirubin, ALP, GGT), US finding of common bile duct dilatation, or has suffered a recent episode of acute pancreatitis. On the other hand, it should not be forgotten that the dissection-free of the cystic duct may be very challenging in the contest of an inflammatory scenario, and that the diagnosis and the management of common duct stones, if the case, should not be addressed as a first priority. It could be much safer in elderly patients presenting with acute cholecystitis to achieve first the source control of infection by quickly removing the gallbladder and to demand the search and the management of bile duct stones in the course. To reduce the risk of biliary injuries, it has been demonstrated the relevance of the “critical view of safety” (CVS), that is a method of identification of the cystic duct and cystic artery during laparoscopic cholecystectomy [24]. CVS identification requires a few methodic steps. Firstly, the hepato-cystic triangle, that is formed by the cystic duct, the common hepatic duct, and inferior edge of the liver, is cleared of fat and fibrous tissue. The common bile duct and common hepatic duct do not need to be exposed. Secondly, the lower one-third of the gallbladder is separated from the liver to expose the liver bed of the gallbladder. Eventually, only two structures should be seen entering the gallbladder: the artery and the cystic duct. Achieving

the steps sequence for CVS may result in easier said than done in some situations, such as local severe inflammation, gangrenous gallbladder, adhesions, and bleeding, all conditions that make CVS not easy to be identified. In these contexts, laparoscopic anterograde cholecystectomy and laparoscopic subtotal cholecystectomy may be valid and safe options. Nonetheless, in case of inability to proceed safely in laparoscopy, conversion to open surgery is mandatory [25, 26].

The Tokyo guidelines have recently been updated to recommend early laparoscopic cholecystectomy in patients with severe cholecystitis (Severity grade III) if appropriate experience is available and if the patients do not have any high-risk predictive factor for morbidities such as jaundice, neurological dysfunction, or respiratory failure [27]. However, some elderly patients with ASA III/IV, performance status 3 to 4, or septic shock remain unfit for surgery. Laparoscopic cholecystectomy is associated with a mortality rate of 0–0.8% in the general population but mortality increases dramatically up to 14–30% in elderly or critically ill patients with comorbid diseases [28]. For elderly patients presenting with AC and unfit for surgery, the first initial approach should be aggressive and based on antibiotic therapy, pain control, careful fluids administration, oxygen supplementation, and monitoring of vital signs. Those responding to medical management are evaluated the following days in order to reassess the risk for surgery. If the re-evaluation confirms the high risk for surgery, patients are considered as patients with chronic cholecystitis and enter a follow-up program. Surgeons should always keep in mind that cholecystolithiasis is a benign condition and that surgery should not be offered at every cost. For those patients in which the initial medical management fails, the drainage of the inflamed gallbladder becomes the next step. Current guidelines recommend percutaneous cholecystostomy for moderate (grade II) or severe (grade III) acute cholecystitis as an effective life-saving method in older or in frail patients who are deemed unfit for surgery [15, 28, 29]. Nevertheless, the percutaneous cholecystostomy is a procedure which may lead to potential and dangerous complications. In a study by Wiggins et al. on 47,500 patients over the age of 80 admitted as an emergency with acute cholecystitis, 89.7% of patients were treated conservatively, 7.5% had cholecystectomy, and 2.8% underwent cholecystostomy. As short-term results, 30-day mortality was significantly increased in the emergency cholecystectomy group (11.6%) compared to those managed conservatively (9.9%). However, this was offset by the long-term benefits of cholecystectomy that showed a lower 1-year mortality (20.8 vs. 27.1% for those managed conservatively). Patients managed by percutaneous cholecystostomy had the worse 30-day and 1-year mortality results (13.4 and 35.0%, respectively). The recent CHOCOLATE study by Loozen et al. analyzed 142 high-risk patients with acute calculous cholecystitis that were randomly allocated to laparoscopic cholecystectomy ($n = 66$) or to percutaneous catheter drainage ($n = 68$) management. They observed that the rate of death did not differ between the laparoscopic cholecystectomy and percutaneous catheter drainage group (3% vs 9%), but major complications (12% vs 65%), reinterventions (12% vs 66%), and recurrent biliary disease (5% vs 53%) all were significantly more frequent in the percutaneous drainage group. In addition, the authors found that the median length of hospital stay was also longer in the latter group (9 days vs

5 days). The conclusion was that laparoscopic cholecystectomy compared with percutaneous catheter drainage has a reduced rate of major complications in high-risk patients with acute cholecystitis [30].

Due to the limits of percutaneous drainage, the decision to place a cholecystostomy should be carefully evaluated case-by-case. When drainage of the gallbladder is advised, a percutaneous transhepatic route under local anesthesia is the preferred method. Specific complications of this procedure account for 3.4% and include bile duct leak, biliary peritonitis, portal or parenchymal vessel injury and bleeding, catheter dislodgement, colon injury, and vagal reaction. The transhepatic route should not be employed in patients with severe liver disease and coagulopathy [28]. The cholecystostomy catheter can be removed between 4 and 6 weeks after its placement, once the biliary tree patency has been proved by a cholangiogram [31, 32].

25.2 Common Bile Duct Stones

The presence of obstructive jaundice needs to be carefully assessed because it reflects a wide spectrum of potentially benign and malignant conditions. These include, but are not limited to, common bile duct (CBD) obstruction from external compression (cholangiocarcinoma, periampullary cancers, gallbladder cancer), choledocholithiasis, and liver failure (e.g., secondary to sepsis). Common bile duct stones occur in about 5–10% of patients with acute cholecystitis [33–36]. The routine use of biochemical tests should be used for the suspicion of common bile duct stones with some limitations. Preoperative magnetic resonance cholangiopancreatography (MRCP), endoscopic US, intraoperative cholangiography, or laparoscopic ultrasound should be performed depending on the local expertise and availability. Common bile duct stones can be removed preoperatively, intraoperatively, or post-operatively according to the local expertise and the instrumentation availability. Endoscopic retrograde cholangiopancreatography (ERCP) and laparoscopic common bile duct exploration (LCBDE) represent the two dominant methods for CBD clearance [37, 38]. Currently, many different strategies have been described for the management of common bile duct stones in patients scheduled for laparoscopic cholecystectomy. The bile duct can be cleared during the same cholecystectomy procedure by a surgical exploration of the duct (LCBDE) or by performing an intraoperative ERCP (iERCP); alternatively, the ERCP may precede or follow the laparoscopic cholecystectomy procedure. LCBDE and iERCP carry the benefit of being performed as a single procedure [39, 40]. The laparoscopic CBD clearance could be done via a trans-cystic or a trans-choledochotomy access depending on the diameter of the CBD, the size and the number of stones, the level of the junction between the CBD and the cystic duct, and the grade of the inflammation of the hepatoduodenal ligament. Choledochoscopy may help surgeons to ascertain the successful clearance of the common bile duct. Although no consensus exists on which between LCBDE and ERCP is the best strategy for the management of common bile duct stones, a decreasing use of LCBDE in the common surgical practice has been recently observed [41, 42]. Surgeons are often reluctant to perform biliary tract surgery in

elderly patients with gallstone disease and in these cases ERCP may suffice [43, 44]. Zheng et al. compared 253 patients younger and 123 patients older than 70 years undergoing LBCDE. They showed that LCBDE was equally successful with a high clearance rate (100% in elderly patients and 98.8% in younger group) and with no significant differences in terms of operating time, intraoperative blood loss, postoperative hospital stay, total costs, overall complication, major bile duct injury, and death. They concluded that LCBDE is safe and effective even in elderly patients [45]. From a practical point of view, the feasibility of LCBDE depends on several factors including surgical expertise, adequate equipment, a patent and not inflamed cystic duct, and common duct stones not larger than the caliber of the cystic duct. Moreover, LCBDE extends the time of the surgical procedure. Thus, it appears reasonable that where the expertise in operative endoscopy is available, ERCP rather than LCBDE becomes the daily practice [46]. The need to place biliary drains such as T-Tubes could reduce the quality of life of an elderly patient and this may be an additional point to favoring ERCP respect to a surgical approach to the main bile duct.

25.3 Acute Cholangitis

Acute cholangitis is defined as acute inflammation and infection of the biliary tree. The dominant cause of acute cholangitis is choledocholithiasis, followed by benign biliary stenosis and cancer [47]. This clinical condition may present with a wide variety of symptoms, ranging from nonspecific findings to severe infection and fatal septic shock. According to the most recent Tokyo guidelines, the severity of acute cholangitis is graded in acute, mild, or severe depending on the patient's general clinical condition and the dysfunction of one or more organs/systems [48]. Most frequently, patients present with grade I disease (54%), while only 11% develop a grade III [47]. The only way to minimize morbidity and mortality is an early diagnosis and a timely and proper treatment. Due to the improvement in the therapeutic options, the mortality of acute cholangitis has been declined and currently is less than 5%. Severe sepsis with multiorgan failure is the main cause of death [3]. An aggressive therapy including NPO, intravenous fluids, antibiotics, and analgesia is the initial step in the management of this life-threatening condition [47]. Large-board antibiotic coverage should be addressed against gram-negative, gram-positive bacteria, and anaerobes. Antibiotics can be tapered on the basis of final culture results. Medical treatment may be sufficient in selected cases of acute cholangitis, but biliary drainage should be considered for all nonresponders to the initial management [29].

Biliary decompression may be achieved by endoscopy, percutaneous drainage, or surgery. The choice of the approach must be based on the etiology of the cholangitis and on the patient's physiological status [49, 50]. Elderly patients with acute cholangitis are often critically ill and emergency decompressive interventions are necessary. Compared to percutaneous transhepatic biliary drainage and emergency surgery (including laparoscopic or open choledocholithotomy) endoscopic

retrograde cholangiopancreatography (ERCP) is the most common and effective interventional method for biliary decompression [51]. Emergency ERCP biliary drainage in older with severe comorbidities is not a procedure free from risks [52]. Complications of ERCP include pancreatitis, hemorrhage, perforation, cholangitis, and cardiorespiratory problems and may occur from 7 to 15% of cases [53]. Emergency surgery decompression of the common duct and T-Tube placement is however burdened by higher rates of morbidity and mortality [54]. Thus, surgery should be offered as a last option therapy. The rate of ERCP-related complications in the elderly are comparable with those of younger patients [55–57], but only a few reports address the role of emergency ERCP for the management of elderly patients with acute cholangitis [54]. Endoscopic retrograde cholangiopancreatography (ERCP) with sphincterotomy has been established as an effective method to treat patients with acute cholangitis [58], but, as already said, it is not a procedure free of adverse events [59]. In elderly patients presenting with acute cholangitis and critically ill, ERCP should be limited to quick drainage of the common duct with a biliary stent insertion, without any attempt to remove the stones. These will be eventually removed by a second endoscopic procedure once the source control has been achieved and the patient's conditions have been restored [60]. In their retrospective review, Tonda et al. compared patients under versus over 80 years old with acute cholangitis undergoing biliary drainage by stent insertion with or without endoscopic sphincterotomy as an initial treatment, and repeated ERCPs for the extraction of residual biliary stones in the patients whose clinical conditions had improved. As a result, the technical success and ERCP-related complication rates were comparable between the two groups except for post-ERCP pancreatitis that was significantly lower in the elderly group [61]. Emergency ERCP for acute cholangitis is a safe and effective procedure in elderly patients. Advanced age is not a contraindication to ERCP. However, informed consent, adequate monitoring during the procedure, prompt detection, and management of ERCP-related complications are crucial.

ERCP cannot be performed in some circumstances, for example, in case of complete biliary obstruction, in patients who have a Roux-en-Y reconstruction, or a periampullary duodenal diverticulum. In such situations, a percutaneous transhepatic biliary drainage could be an option, especially if the biliary tree proximal to the obstruction is dilated. This procedure is rarely used, and it may carry important complications like intraperitoneal hemorrhage, haemobilia, and bile peritonitis. The open surgical approach with drainage of the biliary tree in patients with acute cholangitis should be considered only as a last resort procedure, as it carries a mortality rate of around 30% [31].

Because a scheduled laparoscopic cholecystectomy following emergency ERCP for acute cholangitis secondary to choledocholithiasis has a not negligible risk of complications, the need for definitive surgical treatment should be carefully evaluated and perhaps limited only to patients fit to surgery which suffer recurrent episodes of acute cholangitis [62]. Patients presenting with acute cholangitis due to cancer require different management and should be referred for a definitive treatment following emergency biliary drainage.

25.4 Liver Abscess

Pyogenic liver abscess (PLA) is collection of pus within the liver as a result of an infection. The causes of PLA are thought to be ascending infection from the biliary tract and hematologic spread via the portal vein and hepatic artery. It accounts for almost half of the visceral abscess cases. PLA usually appears in patients with predisposing conditions such as diabetes, hepatobiliary malignancy, or immunosuppression [63]. Life-threatening sepsis can develop in these patients. Along with the rapid aging population, both the incidence of PLA and the mean age of PLA patients have increased steadily in the past several decades [64, 65]. About half of PLAs do not have an identified etiology. Several links between gastrointestinal tract malignancies and PLA have been found [66, 67]. Furthermore, diverticula disease of the colon and hepatobiliary pathology (gallstones, strictures, congenital disease, and cancer) are recognized as causes of PLA [68]. Despite recent improvements, differentiating PLA from hepatic metastasis by imaging studies is still difficult. The differential diagnosis of these two conditions is of paramount importance because the treatment strategies are completely different [69]. Clinical characteristics and outcomes of PLA in elderly patients are insufficiently elucidated. A few studies attempted to investigate the role of age in PLA and have yielded controversial results [70–76]. PLAs may present with atypical symptoms and signs on admission. In elderly patients, lower body temperature and a higher heart rate could be the only clinical manifestations [77]. The most common pathogens are *Escherichia coli*, *Enterococcus*, and *Streptococcus*, being commonly polymicrobial in oncological patients. Infection with *Klebsiella pneumoniae* is the most prevalent in Asia, but it has been increasing in the occidental population [78, 79]. Elderly PLA patients appear to have a slightly lower positive rate on both pus and blood culture than young ones [77]. Imaging studies (ultrasound, CT scan, and MRI with gadolinium) play a crucial role in making the diagnosis. The treatment should be based on the patient's condition and his response to antibiotic therapy, but it depends also on the number and the size of the abscesses, the degree of colliquation, and the presence of septa inside the abscess cavity. Preferred methods of treatment include intravenous broad-spectrum antibiotics and when appropriate, the drainage of the abscess. The most commonly used antibiotics are fluoroquinolones or third-generation cephalosporin in combination with metronidazole [80]. If it is not possible to isolate the agent to obtain a cultural examination and antibiotics sensibility test, empiric antibiotics should be the first choice. Surgical drainage may be required in case of larger and multilocular abscesses, failure of percutaneous drainage, or when surgical treatment of the underlying cause of PLA is needed [80, 81]. Surgical drainage or resection could be performed via open or laparoscopic approach, according to the grade of experience of the surgeon, available resources, and patient's clinical conditions.

The impact of aging on outcomes of patients with PLA remains unclear. Zhang et al. showed from a cohort of 332 patients that there were no significant differences in the therapeutic procedures performed between young and elderly PLA patients (antibiotics alone vs percutaneous drainage vs surgical drainage). Moreover, the authors demonstrated that older and younger PLA patients had comparable results [77]. If untreated,

PLA may reach a 100% mortality. Moreover, around 40% of cases with PLA may develop local or systemic complications, the most common being generalized sepsis and pleural effusion. Other complications include rupture of the liver abscess to the peritoneal cavity, thrombosis of the portal vein or of the hepatic veins, IVC occlusion, development of pseudoaneurysm of the hepatic artery, haemobilia, and, very rarely, the appearance of a fistula to the portal vein or to the hepatic veins. When the PLA is properly treated, complications are contained between 2.5 and 14% [82]. Thus, surgeons need to be on high alert when a PLA in elderly patients is diagnosed. A multidisciplinary approach may be reasonable in order to achieve source control and to address comorbidities. If adequately managed, older PLA patients have outcomes comparable to their younger counterparts with a high rate of cure achieved in both groups.

References

1. Yokoe M, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Gomi H, et al. New diagnostic criteria and severity assessment of acute cholecystitis in revised Tokyo guidelines. *J Hepatobiliary Pancreat Sci.* 2012;19(5):578–85.
2. Bollen TL, van Santvoort HC, Besselink MG, van Leeuwen MS, Horvath KD, Freeny PC, et al. The Atlanta classification of acute pancreatitis revisited. *Br J Surg.* 2008;95(1):6–21.
3. Kiriya S, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Pitt HA, et al. New diagnostic criteria and severity assessment of acute cholangitis in revised Tokyo guidelines. *J Hepatobiliary Pancreat Sci.* 2012;19(5):548–56.
4. Kimura Y, Takada T, Kawarada Y, Nimura Y, Hirata K, Sekimoto M, et al. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo guidelines. *J Hepatobiliary Pancreat Surg.* 2007;14(1):15–26.
5. Pisano M, et al. 2017 WSES and SICG guidelines on acute calculous cholecystitis in elderly population. *World J Emerg Surg.* 2019;14:10.
6. Costa G, Massa G, ERASO (Elderly Risk Assessment for Surgical Outcome) Collaborative Study Group. Frailty and emergency surgery in the elderly: protocol of a prospective, multi-center study in Italy for evaluating perioperative outcome (The FRAILESEL Study). *Updates Surg.* 2018;70(1):97–104.
7. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol.* 1994;47(11):1245–51.
8. Rockwood K, Mitnitski A. Frailty defined by deficit accumulation and geriatric medicine defined by frailty. *Clin Geriatr Med.* 2011;27(1):17–26; ACS NSQIP SRC. <http://riskcalculator.facs.org/>
9. Riall TS, Zhang D, Townsend CM, Kuo Y-F, Goodwin JS. Failure to perform cholecystectomy for acute cholecystitis in elderly patients is associated with increased morbidity, mortality, and cost. *J Am Coll Surg.* 2010;210:668–77.
10. Gurusamy KS, Rossi M, Davidson BR. Percutaneous cholecystostomy for high-risk surgical patients with acute calculous cholecystitis. *Cochrane Database Syst Rev.* 2013;2013:CD007088.
11. Kortram K, van Ramshorst B, Bollen TL, Besselink MGH, Gouma DJ, Karsten T, et al. Acute cholecystitis in high risk surgical patients: percutaneous cholecystostomy versus laparoscopic cholecystectomy (CHOCOLATE trial): study protocol for a randomized controlled trial. *Trials.* 2012;13:7. BioMed Central Ltd.
12. Bates AT, Divino C. Laparoscopic surgery in the elderly: a review of the literature. *Aging Dis.* 2015;6:149–55.
13. Magnuson TH, Ratner LE, Zenilman ME, Bender JS. Laparoscopic cholecystectomy: applicability in the geriatric population. *Am Surg.* 1997;63:91–6.

14. Annamaneni RK, Moraitis D, Cayten CG. Laparoscopic cholecystectomy in the elderly. *JLSLS*. 9:408–10.
15. Mayol J, Martinez-Sarmiento J, Tamayo FJ, Fernández-Represa JA. Complications of laparoscopic cholecystectomy in the ageing patient. *Age Ageing*. 1997;26:77–81.
16. Ansaloni L, Pisano M, Coccolini F, Peitzmann AB, Fingerhut A, Catena F, et al. 2016 WSES guidelines on acute calculous cholecystitis. *World J Emerg Surg*. 2016;11:25.
17. Chandler CF, Lane JS, Ferguson P, Thompson JE, Ashley SW. Prospective evaluation of early versus delayed laparoscopic cholecystectomy for treatment of acute cholecystitis. *Am Surg*. 2000;66:896–900.
18. Gutt CN, Encke J, Köninger J, Harnoss J-C, Weigand K, Kipfmüller K, et al. Acute cholecystitis: early versus delayed cholecystectomy, a multicenter randomized trial (ACDC study, NCT00447304). *Ann Surg*. 2013;258:385–93.
19. Zafar SN, Obirieze A, Adesibikan B, Cornwell EE, Fullum TM, Tran DD. Optimal time for early laparoscopic cholecystectomy for acute cholecystitis. *JAMA Surg*. 2015;150:129–36.
20. Johner A, Raymakers A, Wiseman SM. Cost utility of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Surg Endosc*. 2013;27:256–62.
21. Brooks KR, Scarborough JE, Vaslef SN, Shapiro ML. No need to wait: an analysis of the timing of cholecystectomy during admission for acute cholecystitis using the American College of Surgeons National Surgical Quality Improvement Program database. *J Trauma Acute Care Surg*. 2013;74:167–73; 173–4.
22. Hauer-Jensen M, Karesen R, Nygaard K, Solheim K, Amlie EJ, Havig O, et al. Prospective randomized study of routine intraoperative cholangiography during open cholecystectomy: long-term follow-up and multivariate analysis of predictors of choledocholithiasis. *Surgery*. 1993;113(3):318–23.
23. Ford JA, Soop M, Du J, Loveday BP, Rodgers M. Systematic review of intraoperative cholangiography in cholecystectomy. *Br J Surg*. 2012;99(2):160–7.
24. Strasberg SM, Brunt LM. Rationale and use of the critical view of safety in laparoscopic cholecystectomy. *J Am Coll Surg*. 2010;211:132–8.
25. Tang B, Cuschieri A. Conversions during laparoscopic cholecystectomy: risk factors and effects on patient outcome. *J Gastrointest Surg*. 2006;10:1081–91.
26. Halachmi S, DiCastro N, Matter I, Cohen A, Sabo E, et al. Laparoscopic cholecystectomy for acute cholecystitis: how do fever and leucocytosis relate to conversion and complications? *Eur J Surg*. 2000;166:136–40.
27. Yokoe M, et al. Tokyo guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci*. 2018;25(1):41–5.
28. Bakkaloglu H, Yanar H, Guloglu R, Taviloglu K, Tunca F, Aksoy M. Ultrasound guided percutaneous cholecystostomy in high-risk patients for surgical intervention. *World J Gastroenterol*. 2006;12(44):7179–82.
29. Miura F, Takada T, Kawarada Y, Nimura Y, Wada K, Hirota M. Flowcharts for the diagnosis and treatment of acute cholangitis and cholecystitis: Tokyo guidelines. *J Hepatobiliary Pancreat Surg*. 2007;14(1):27–34.
30. Loozen CS, van Santvoort HC, van Duijvendijk P, et al. Laparoscopic cholecystectomy versus percutaneous catheter drainage for acute cholecystitis in high risk patients (CHOCOLATE): multicentre randomised clinical trial. *BMJ*. 2018;363:k3965.
31. Lai EC, Tam PC, Paterson IA, Ng MM, Fan ST, Choi TK, Wong J. Emergency surgery for severe acute cholangitis. The high-risk patients. *Ann Surg*. 1990;211:55–9.
32. Venara A, Carretier V, Lebigot J, Lermite E. Technique and indications of percutaneous cholecystostomy in the management of cholecystitis in 2014. *J Visc Surg*. 2014;151:435–9.
33. Peng WK, Sheikh Z, Paterson-Brown S, Nixon SJ. Role of liver function tests in predicting common bile duct stones in acute calculous cholecystitis. *Br J Surg*. 2005;92:1241–7.
34. Khalfallah M, Dougaz W, Bedoui R, Bouasker I, Chaker Y, Nouira R, et al. Validation of the Lacaine-Huguier predictive score for choledocholithiasis: prospective study of 380 patients. *J Visc Surg*. 2012;149(1):e66–72.

35. Ko CW, Lee SP. Epidemiology and natural history of common bile duct stones and prediction of disease. *Gastrointest Endosc.* 2002;56(6 Suppl):S165–9.
36. Csendes A, Fernandez M, Uribe P. Bacteriology of the gallbladder bile in normal subjects. *Am J Surg.* 1975;129(6):629–31.
37. Tzovaras G, Baloyiannis I, Zachari E, Symeonidis D, Zacharoulis D, Kapsoritakis A, et al. Laparoendoscopic rendezvous versus preoperative ERCP and laparoscopic cholecystectomy for the management of cholecysto-choledocholithiasis: interim analysis of a controlled randomized trial. *Ann Surg.* 2012;255(3):435–9.
38. Gurusamy K, Sahay SJ, Burroughs AK, Davidson BR. Systematic review and meta-analysis of intraoperative versus preoperative endoscopic sphincterotomy in patients with gallbladder and suspected common bile duct stones. *Br J Surg.* 2011;98(7):908–16.
39. Rogers SJ, Cello JP, Horn JK, Siperstein AE, Schechter WP, Campbell AR, et al. Prospective randomized trial of LC + LCBDE vs ERCP/S + LC for common bile duct stone disease. *Arch Surg.* 2010;145(1):28–33.
40. Li MK, Tang CN, Lai EC. Managing concomitant gallbladder stones and common bile duct stones in the laparoscopic era: a systematic review. *Asian J Endosc Surg.* 2011;4(2):53–8.
41. Wandling MW. Nationwide assessment of trends in choledocholithiasis management in the United States from 1998 to 2013. *JAMA Surg.* 2016;151(12):1125–30.
42. Palermo M, Duza G, Caviglia ML, De Innocentis N, Egan P, Fiscella G, Moran M, Prieto J, Sousa M, Garcia R. Treatment of bile duct stones by laparoscopy, endoscopy or combined approaches. *Acta Gastroenterol Latinoam.* 2015;45:90–6.
43. Costi R, DiMauro D, Mazzeo A, Boselli AS, Contini S, Violi V, Roncoroni L, Sarli L. Routine laparoscopic cholecystectomy after endoscopic sphincterotomy for choledocholithiasis in octogenarians: is it worth the risk? *Surg Endosc.* 2007;21:41–7.
44. Weber DM. Laparoscopic surgery: an excellent approach in elderly patients. *Arch Surg.* 2003;138:1083–8.
45. Zheng C, et al. Laparoscopic common bile duct exploration: a safe and definitive treatment for elderly patients. *Surg Endosc.* 2017;31:2541–7.
46. Baucom RB, Feurer ID, Shelton JS, Kummerow K, Holzman MD, Poulouse BK. Surgeons, ERCP, and laparoscopic common bile duct exploration: do we need a standard approach for common bile duct stones? *Surg Endosc.* 2016;30:414–23.
47. Butte JM, et al. Hepato-pancreato-biliary emergencies for the acute care surgeon: etiology, diagnosis and treatment. *World J Emerg Surg.* 2015;10:13.
48. Itoi T, Tsuyuguchi T, Takada T, et al. TG13 indications and techniques for biliary drainage in acute cholangitis (with videos). *J Hepatobiliary Pancreat Sci.* 2013;20:71–80.
49. Lau WY, Chu KW, Yuen WK, Poon GP, Hwang JS, Li AK. Operative choledochoscopy in patients with acute cholangitis: a prospective, randomized study. *Br J Surg.* 1991;78(10):1226–9.
50. Lee DW, Chan AC, Lam YH, Ng EK, Lau JY, Law BK, et al. Biliary decompression by nasobiliary catheter or biliary stent in acute suppurative cholangitis: a prospective randomized trial. *Gastrointest Endosc.* 2002;56(3):361–5.
51. Zhang X, Li G, Pan L, Chen Y, Shi R, Xu W, Zhou K, Cheng Y, Feng Y, Zhou A, Zhao K. The efficacy and safety of one-stage endoscopic treatment for ascending acute cholangitis caused by choledocholithiasis with severe comorbidities. *Surg Endosc.* 2020;34(9):3963–70.
52. Yun DY, Han J, Oh JS, Park KW, Shin IH, Kim HG. Is endoscopic retrograde cholangiopancreatography safe in patients 90 years of age and older? *Gut Liver.* 2014;8(5):552–6.
53. Anderson MA, et al. Complications of ERCP. *Gastrointest Endosc.* 2012;75:467–73.
54. Hui CK, Liu CL, Lai KC, Chan SC, Hu WH, Wong WM, Cheung WW, Ng M, Yuen MF, Chan AO, Lo CM, Fan ST, Wong BC. Outcome of emergency ERCP for acute cholangitis in patients 90 years of age and older. *Aliment Pharmacol Ther.* 2004;19:1153–8.
55. Cameron JL, Cameron AM. *Current surgical therapy.* 12th ed.
56. Garcia CJ, Lopez OA, Islam S, Othman M, Jia Y, Mulla ZD, Zuckerman MJ. Endoscopic retrograde cholangiopancreatography in the elderly. *Am J Med Sci.* 2016;351:84–90.

57. Rodríguez-González FJ, Naranjo-Rodríguez A, Mata-Tapia I, Chicano-Gallardo M, Puente-Gutierrez JJ, López-Vallejos P, Hervás-Molina AJ, de Dios-Vega JF. ERCP in patients 90 years of age and older. *Gastrointest Endosc.* 2003;58:220–5.
58. Siegel JH, Kasmin FE. Biliary tract diseases in the elderly: management and outcomes. *Gut.* 1997;41:433–5.
59. Andriulli A, Loperfido S, Napolitano G, Niro G, Valvano MR, Spirito F, Pilotto A, Forlano R. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. *Am J Gastroenterol.* 2007;102:1781–8.
60. Park CS, Jeong HS, Kim KB, et al. Urgent ERCP for acute cholangitis reduces mortality and hospital stay in elderly and very elderly patients. *Hepatobiliary Pancreat Dis Int.* 2016;15:619–25.
61. Tohda G, et al. Efficacy and safety of emergency endoscopic retrograde cholangiopancreatography for acute cholangitis in the elderly. *World J Gastroenterol.* 2016;22(37):8382–8.
62. Severance SE, Feizpour C, Feliciano DV, Coleman J, Zarzaur BL, Rozycki GF. Timing of cholecystectomy after emergent endoscopic retrograde cholangiopancreatography for cholangitis. *Am Surg.* 2019;85(8):895–9.
63. Chaubal N, Joshi M, Bam A, Chaubal R. Contrast enhanced ultrasound of focal liver lesions. *Semin Roentgenol.* 2016;51:334–57.
64. Meddings L, Myers RP, Hubbard J, Shaheen AA, Laupland KB, Dixon E, Coffin C, Kaplan GG. A population-based study of pyogenic liver abscesses in the United States: incidence, mortality, and temporal trends. *Am J Gastroenterol.* 2010;105(1):117–24.
65. Tsai FC, Huang YT, Chang LY, Wang JT. Pyogenic liver abscess as endemic disease. *Taiwan Emerg Infect Dis.* 2008;14(10):1592–600.
66. Jeong SW, Jang JY, Lee TH, et al. Cryptogenic pyogenic liver abscess as the herald of colon cancer. *J Gastroenterol Hepatol.* 2012;27:248–55.
67. Johanssen EC, Sifri CD, Madoff LC. Pyogenic liver abscesses. *Infect Dis Clin N Am.* 2000;14:547–63. vii
68. Murarka S, Pranav F, Dandavate V. Pyogenic liver abscess secondary to disseminated streptococcus anginosus from sigmoid diverticulitis. *J Glob Infect Dis.* 2011;3(1):79–81.
69. Bachler P, Baladron MJ, Menias C, et al. Multimodality imaging of liver infections: differential diagnosis and potential pitfalls. *Radiographics.* 2016;36:1001–23.
70. Wi JW, Cho EA, Jun CH, Park SY, Park CH, Joo YE, Kim HS, Choi SK, Rew JS, Jung SI. Clinical characteristics and outcomes of pyogenic liver abscess in elderly Korean patients. *Korean J Gastroenterol.* 2015;66(1):27–32.
71. Law ST, Li KK. Older age as a poor prognostic sign in patients with pyogenic liver abscess. *Int J Infect Dis.* 2013;17(3):e177–84.
72. Chen SC, Lee YT, Yen CH, Lai KC, Jeng LB, Lin DB, Wang PH, Chen CC, Lee MC, Bell WR. Pyogenic liver abscess in the elderly: clinical features, outcomes and prognostic factors. *Age Ageing.* 2009;38(3):271–6; discussion.
73. Kang SC, Hwang SJ. Impact of advanced age on inpatients with pyogenic liver abscess in Taiwan: a nationwide claim-based analysis. *J Chin Med Assoc.* 2011;74(12):539–43.
74. Alvarez JA, Gonzalez JJ, Baldonado RF, Sanz L, Junco A, Rodríguez JL, Martínez MD. Pyogenic liver abscesses: a comparison of older and younger patients. *HPB (Oxford).* 2001;3(3):201–6.
75. Smoger SH, Mitchell CK, McClave SA. Pyogenic liver abscesses: a comparison of older and younger patients. *Age Ageing.* 1998;27(4):443–8.
76. Peris J, Bellot P, Roig P, Reus S, Carrascosa S, Gonzalez-Alcaide G, Palazon JM, Ramos JM. Clinical and epidemiological characteristics of pyogenic liver abscess in people 65 years or older versus people under 65: a retrospective study. *BMC Geriatr.* 2017;17(1):16.
77. Zhang J, et al. Comparison of clinical characteristics and outcomes of pyogenic liver abscess patients < 65 years of age versus ≥ 65 years of age. *BMC Infect Dis.* 2019;19:23.
78. Qian Y, Wong CC, Lai S, Chen H, He X, Sun L, Wu J, Zhou J, Yu J, Liu W, et al. A retrospective study of pyogenic liver abscess focusing on *Klebsiella pneumoniae* as a primary pathogen in China from 1994 to 2015. *Sci Rep.* 2016;6:38587.

79. Du ZQ, Zhang LN, Lu Q, Ren YF, Lv Y, Liu XM, Zhang XF. Clinical characteristics and outcome of pyogenic liver abscess with different size: 15- year experience from a single center. *Sci Rep.* 2016;6:35890.
80. Sotto Mayor J, Robalo MM, Pacheco AP, Esperança S. Pyogenic liver abscess: uncommon presentation. *BMJ Case Rep.* 2016;2016:bcr2016214841.
81. Lardiere-Deguelte S, Ragot E, Amroun K, Piardi T, Dokmak S, Bruno O, Appere F, Sibert A, Hoeffel C, Sommacale D, et al. Hepatic abscess: diagnosis and management. *J Visc Surg.* 2015;152(4):231–43.
82. Pinto E, Sousa M, Costa A. Pyogenic liver abscesses: from the interventional radiologist point of view. *Rev Clin Hosp Prof Dr Fernando Fonseca.* 2013;1:27–33.