Hotspots and difficulties of biliary surgery in older patients

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Abstract

With the accelerated aging society in China, the incidence of biliary surgical diseases in the elderly has increased significantly. The clinical characteristics of these patients indicate that improving treatment outcomes and realizing healthy aging are worthy of attention. How to effectively improve the treatment effect of geriatric biliary surgical diseases has attracted widespread attention. This paper reviews and comments on the hotspots and difficulties of biliary surgery in older patients from six aspects: (1) higher morbidity associated with an aging society, (2) prevention and control of pre-operative risks, (3) extending the indications of laparoscopic surgery, (4) urgent standardization of minimally invasive surgery, (5) precise technological progress in hepatobiliary surgery, and (6) guarantee of peri-operative safety. It is of great significance to fully understand the focus of controversy, actively make use of its favorable factors, and effectively avoid its unfavorable factors, for further improving the therapeutic effects of geriatric biliary surgical diseases, and thus benefits the vast older patients with biliary surgical diseases. Accordingly, a historical record with the highest age of 93 years for laparoscopic transcystic common bile duct exploration has been created by us recently.
Keywords: Biliary tract diseases; Biliary surgery; Minimally invasive surgery; Laparoscopic surgery; Precise hepatobiliary surgical technology; Elderly

Introduction

China is entering a deep aging society, with 14.2% of the population aged ≥65 years. Biliary diseases requiring surgery in older patients have increased, with morbidity of 8% to 11%, which has attracted widespread attention.[1] Older patients, due to a decline in body and immune functions, have clinical characteristics of rapid disease progression, more pre-operative comorbidity, poor surgical tolerance, high surgical risk, post-operative complications, and high mortality. Although the technological progress in geriatric biliary surgery is minimally invasive and precise, there is still a lack of consensus on their indications and standardized procedures, and there are no effective prevention and treatment measures to ensure their peri-operative safety in geriatric biliary diseases requiring surgery. Therefore, there is a need to actively improve the treatment of biliary diseases in older patients.

Based on our clinical experience in treatment of geriatric biliary surgical diseases,[2,3] along with the latest literature reports,[4-6] the hotspots and difficulties are discussed in this review.

Higher morbidity associated with an aging society

Aging is the main trend in population development. At present, one-third of the countries and regions in the world have a higher number of elderly people. It is estimated that, by the middle of this century, the world will consist of 2 billion older people. The issue of aging has greatly affected all generations of the society.

Since October 1999, the proportion of older population in China has reached 10%, marking its entry into an aging society. According to the data released by the National Bureau of Statistics of China on January 17, 2022, the

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population aged ≥60 years is 267.36 million, accounting for 18.90% of the total population. Among them, the population aged ≥65 years has reached 200.56 million, accounting for 14.2% of the national population. This indicates that China has entered a deep aging society (population aged ≥65 years accounts for >14%).[7] It is estimated that, by the middle of this century, China's older population is likely to grow by >400 million and may account for 20% of the global older population, becoming the country with the largest older population in the world.[8]

An increasing pace of aging and fluctuating population trends in China poses serious challenges for population health, which makes predicting future trends increasingly important.[9,10] With the increase in the aging population, geriatric biliary diseases requiring surgery, mainly to treat stones, inflammation, and tumors, have become frequent in the population of China, with a morbidity rate of 8% to 11%, which warrants more attention. Therefore, there is widespread attention to actively improve the treatment of biliary diseases in older patients.

Prevention and control of pre-operative risks in geriatric biliary diseases requiring surgery

Based on the above mentioned clinical characteristics of geriatric biliary diseases requiring surgery, it is necessary to take appropriate measures to actively prevent and control their pre-operative risks. It has been reported that the morbidity of coexisting diseases in older patients with biliary diseases is as high as 65% to 90%, often combined with one or more coexisting diseases.[11] The most serious pre-operative risks come from three most common coexisting diseases, such as hypertension, coronary heart disease (CHD), and diabetes.

For coexisting hypertension, it is suggested that thiazide diuretics, calcium channel blockers, beta-blockers, and other anti-hypertensive drugs should be taken before surgery. Because peri-operative hypertension can enhance peri-operative bleeding and induce myocardial ischemia, acute myocardial infarction (AMI), stroke, renal failure, and other complications, the purpose of peri-operative blood pressure control is to ensure the perfusion of important organs, reduce cardiac post-load, and maintain cardiac function. It was recommended that a magnitude of 10% to 20% fluctuation range based on the baseline blood pressure is an optimal blood pressure target for high-risk patients.[12] The intra-operative blood pressure fluctuation range does not exceed 30% of the basic blood pressure.

For coexisting CHD, active evaluation of peri-operative cardiac function in older patients is important for maintaining stable peri-operative cardiac function and avoiding the occurrence and development of cardiac events. Cardiac function evaluations can be carried out by echocardiography, biomarkers of myocardial injury, biomarkers of heart failure, cardiac magnetic resonance imaging (MRI), cardiac computed tomography (CT), gated single-photon emission CT, myocardial perfusion imaging, and other examination methods,[13] of which the first three are the most commonly used and convenient for repetition. If cardiac dysfunction or arrhythmia can be controlled by drugs, cardiac compensatory function is better, and if ejection fraction is >60%, surgical treatment can be considered. In patients with symptoms of AMI, the serum levels of high sensitivity troponin-I (Hs-TnI), creatine kinase isoenzyme (CK-MB), myoglobin (MYO), and B-type natriuretic peptide should be measured urgently to establish the severity of myocardial injury and heart failure. If the levels of Hs-TnI, CK-MB, and MYO are increased, diagnosis of AMI is suggested, which should be actively treated, and the operation should be carried out carefully or postponed.

For coexisting diabetes, disorders of glucose metabolism and insulin resistance caused by surgical stress are more significant and even produce ketone bodies or cause non-ketoacidosis hypertonic. Therefore, oral hypoglycemic drugs and medium- and long-acting insulin should be stopped before the operation, and ordinary insulin should be used instead. According to the expert's consensus on peri-operative blood glucose management,[14] the optional control of peri-operative blood glucose is 8 to 10 mmol/L fasting or premeal blood glucose, 8 to 12 mmol/L random blood glucose in 2 h after a meal or when unable to eat, and <15 mmol/L short term blood glucose is also acceptable; the general control is 6 to 8 mmol/L fasting or premeal blood glucose, and 8 to 10 mmol/L random blood glucose in 2 h after a meal or when unable to eat; the strictly control is 4.4 to 6.0 mmol/L fasting or premeal blood glucose, and 6 to 8 mmol/L random blood glucose in 2 h after a meal or when unable to eat for patients with severe diabetes. Recently, Vogt and Bally[15] suggested that peri-operative blood glucose levels should be kept <10.0 mmol/L to avoid hypoglycemia, with the optimal range being 5.6 to 10.0 mmol/L. It should be emphasized that the complexity of peri-operative glucose management requires multidisciplinary cooperation, standardized operating procedures, and clinical continuity along the surgical pathway. If the pre-operative glycosylated hemoglobin level is ≤7%, it indicates that in the previous 3 months, the blood glucose has been well controlled, and the risk of peri-operative abnormal blood glucose is low. If the pre-operative glycosylated hemoglobin level is ≥8.5%, postponement of elective surgery should be considered.

Broadening the indications for laparoscopic surgery in older patients with biliary disease

The continuous improvement of laparoscopic surgical techniques and gradual broadening of their indications have removed some contraindications, such as a history of abdominal laparotomy; and the traditional view that laparotomy is necessary in older patients with biliary diseases; such as Mirizzi syndrome, concomitant portal hypertension, and pneumoperitoneum.

History of abdominal laparotomy

A history of upper abdominal surgery, especially in the biliary tract, due to different degrees of abdominal adhesion, is usually listed as a contraindication for laparoscopic biliary surgery to avoid abdominal organ injury. With the continuous progress in laparoscopic technology, there are more reports of successful

laparoscopic biliary surgery for patients with a history of upper abdominal laparotomy or even open biliary surgery.[16,17] Pneumoperitoneum establishment, adhesion separation, and common bile duct (CBD) identification are regarded as the three main difficulties of laparoscopic biliary reoperation, and step-by-step and subtle manipulations are the key to overcome these difficulties.[18] Even for the patients with biliary intestinal anastomotic stenosis after pancreaticoduodenectomy, laparoscopic surgery can be used. Our experience[19] is that (1) the first puncture site is at least 2 cm away from the original open incision because there is generally intestinal or omental adhesion below the original surgical incision, which often exceeds the length of the incision by 2 to 5 cm; (2) when the laparoscope enters the abdominal cavity, if it is difficult to insert the laparoscope because of encapsulated adhesion, we should carefully look for the loose adhesion tissue gap or non-vascular area, use the lens to pass through the adhesion, and assist in separating the adhesion through the auxiliary puncture hole, until the operation site is fully exposed; (3) when separating the adhesion of important organs, the adhesion levels should be clearly identified, and the combination of blunt and sharp separation should be skillfully used, so as to effectively prevent direct injury or delayed electrical injury of adhesive organs.

Mirizzi syndrome

Mirizzi syndrome is a rare complication of cholecystolithiasis, accounting for about 1% of gallstones. The therapeutic principle is to remove the gallbladder and the stones, relieve the obstruction, and repair the CBD. The key to the operation is to correct the existing CBD stenosis and avoid iatrogenic bile duct injury. In the past, Mirizzi syndrome has been listed as a contraindication for laparoscopic surgery. In recent years, with the rapid development of laparoscopic technology, there are more reports of laparoscopic surgery for treatment of Mirizzi syndrome[20,21] and even some reports on the direct use of laparoscopic Roux-en-Y cholangiojejunostomy for the treatment of types III and IV Mirizzi syndrome. Sun[22] reported that for type III Mirizzi syndrome, during the operation, the fistula or ampulla wall should be fully retained to be used for repairing bile duct defects, and cholangiojejunostomy should be avoided as much as possible. For type IV Mirizzi syndrome, laparoscopic Roux-en-Y cholangiojejunostomy can be used as the preferred method for repair and shaping of the CBD with T-tube support drainage. However, cholangiojejunostomy can only be used as a remedial measure for the complete disconnection or poor continuity of the CBD.

Portal hypertension

In patients with biliary diseases requiring surgery, complicated with cirrhosis and portal hypertension, due to liver atrophy and gallbladder bed displacement caused by cirrhosis, it is difficult to dissect and expose the gallbladder and extrahepatic bile duct. Once bleeding occurs in the gallbladder bed during the operation, it is often difficult to control the bleeding because of the high portal vein pressure. There are a large number of varicose veins at the hepatoduodenal ligament, with extensive congestion in the hepatic portal area, which is prone to uncontrollable massive bleeding. Abdominal bleeding, varicose vein rupture, ascites aggravation, and abdominal infection easily occur after the operation, which increases the incidence of post-operative complications and even mortality. Therefore, biliary diseases complicated with portal hypertension in patients were defined as surgical contraindications in the early stage of laparoscopic biliary surgery. With the development of laparoscopic technology, the contraindication has been gradually removed, but it should be emphasized that the disease status needs to be evaluated objectively, comprehensively, and accurately before the operation. In principle, surgery should be avoided for high-risk patients, and it should not be rejected for those with reasonable risk.[23,24] Our experience is that on the basis of strictly mastering the above principles and on the premise of preparing hemostatic drugs such as plasma, prothrombin complex, and fibrinogen before the operation, it is safe and feasible to perform laparoscopic biliary surgery.

Pneumoperitoneum

Laparoscopic biliary surgery usually requires the establishment of CO_2 pneumoperitoneum to ensure visual field exposure and easy operation, but pneumoperitoneum can cause adverse effects on the respiratory, circulatory, and other systems, especially in older patients who cannot tolerate pneumoperitoneum due to severe cardiac and pulmonary insufficiency. To overcome the limitation of pneumoperitoneum, laparoscopic biliary surgery by means of a gasless laproscopic device, abdominal wall lift with low-pressure pneumoperitoneum, and double-vision gasless laparoscopy was developed.[25] Fu *et al*[26] reported that gasless laproscopic cholecystectomy (LC) is advantageous in older patients or those with cardiopulmonary dysfunction. Guo *et al*[27] reported that LC by abdominal wall lift with low-pressure pneumoperitoneum (4–6 mmHg) does not affect respiratory and circulatory functions, provides better surgical fields and reduces the operation duration, and is worthy of being used in older patients undergoing cholecystectomy. Double-vision gasless LC requires an incision in the abdominal wall (2.0–2.5 cm) and placement of retractors with a camera lens and light source, which is not minimally invasive and has the problem of poor exposure field. Therefore, it is not recommended to promote its application. It should be pointed out that the disadvantage of gasless laparoscopic surgery is its difficulty in exposing the operation field. Different from the circular arch space formed by CO_2 pneumoperitoneum, the gasless laparoscopic device makes the operation space between the abdominal wall and organs trapezoid, which can only expose the local area. However, the same effect as CO_2 pneumoperitoneum can be achieved through patient position adjustment of the gasless laparoscopic device.

Urgent standardization of minimally invasive surgery in geriatric biliary diseases requiring surgery

Although various minimally invasive biliary surgical procedures are widely used, there is still a lack of consensus on some methods, such as the advantages and disadvantages of endoscopic sphincterotomy (EST); the laparoscopic transcystic approach with microincision of

the cystic duct confluence in common bile duct exploration (LTM-CBDE)[28]; the controversy of choledochoscopic gallbladder-preserving cholecystolithotomy (CGPC)[29]; and the merits and demerits of the Da Vinci surgical system. Therefore, it is necessary to actively explore and formulate the norms for the relevant surgical methods, especially for older patients with biliary diseases requiring surgery, so as to improve the therapeutic effect of minimally invasive surgery, while avoiding the potential hidden dangers and risks.

Advantages and disadvantages of EST

In 1974, Classen and Kawai reported the success of EST for treatment of residual biliary stones, setting a precedent for endoscopic surgery. After more than 40 years of application and development, EST has become a safe and reliable technique. Nearly 90% of extrahepatic bile duct stones can be removed by EST.[30] However, EST destroys the function of the sphincter of Oddi, which can cause post-operative duodenal fluid reflux and increase the risk of reflux cholangitis, recurrent CBD stones, and even cholangiocarcinoma. In particular, it should be pointed out that with the extensive development of EST, some serious complications have arised, such as the indications of EST are not strictly followed, and the sphincterotomy approach is becoming more and more randomized, which may destroy the physiological function of the Oddi sphincter, making "minimally invasive" surgery a "giant invasive" surgery. Therefore, protection of the structure and function of the sphincter of Oddi should be paid more attention. Ye *et al*[31] recommend endoscopic papillary balloon dilatation (EPBD) as the first choice for removal of small CBD stones, which has a lower bleeding risk than EST, as EPBD is equivalent to EST plus balloon dilatation in stone removal efficiency and complication rates. Zeng and Dong[32] suggested that patients with iatrogenic injury of the sphincter of Oddi should be treated with transduodenal sphincteroplasty to restore the structural integrity of the sphincter and reduce biliopancreatic duct complications secondary to loss of function. Recently, Wang *et al*[33] reported that endoscopic endoclip papilloplasty (EEPP) had accelerated and improved the papillary healing after EST and preserved the physiological function of the sphincter of Oddi. The importance of this report is that EEPP may be a safe and potentially beneficial procedure in reducing post-EST complications.

Recent advancements in technology and the development of the SpyGlass system have led to an increased use of cholangioscopy. It is already known that the SpyGlass system is beneficial in patients with difficult bile duct stones and indeterminate biliary lesions through the use of targeted lithotripsy and visually guided biopsy. Cholangioscopy overall has similar complication rates compared with other standard endoscopic retrograde cholangioscopy techniques, but these may show higher rates of cholangitis.[34]

LTM-CBDE

With the popularization and improvement of laparoscopic and choledochoscopic technology, laparoscopic transcystic common bile duct exploration (LTCBDE) has become an important surgical method for minimally invasive treatment of cholecystolithiasis complicated with choledocholithiasis, with the main advantage of avoiding CBD incision and T-tube placement and reducing the risk of biliary stricture and bile leakage. Recently, a 93-year-old female patient with acute calculous cholecystitis (ACC) and choledocholithiasis who underwent emergency LC plus LTCBDE successfully in Beijing Electric Power Hospital on March 4, 2022, is shown in [Figure 1]. She was discharged from the hospital 7 days after the operation and is leading a healthy life. It is reported that the oldest patient for LTCBDE is aged 87 years abroad[35] and 89 years in China.[36]

However, LTCBDE is not applicable to all patients with cholecystolithiasis combined with choledocholithiasis. For patients with more and/or large CBD stones, slender and twisted cystic duct, and variation in confluence of the CBD and cystic duct, LTCBDE is restricted; so, its indications and contraindications should be strictly controlled. Chen *et al*[37] suggested that for patients with a small cystic duct making choledochoscopy difficult and large CBD stones (diameter >1 cm) that are difficult to remove through the cystic duct, microincision of the confluent part of the CBD and cystic duct can be used to expand the incision, after removing the stones, suturing the microincision of the confluence. Niu *et al*[28] suggested that LTM-CBDE, a modified form of LTCBDE, is a safe and effective treatment for older patients with choledocholithiasis. Some researchers have suggested that LTM-CBDE can cut the confluence of the cystic duct and remove the stones through the side wall of the CBD, which is a concept of disguised displacement and should be abandoned. Our experience is that, although the microincision of the cystic duct confluence in LTM-CBDE deviates from the original intention of LTCBDE, it is still worth trying as a measure to improve the success rate of LTCBDE. The key lies in whether to place the T-tube during the operation, based on whether inflammation of the CBD is serious, whether the stones are removed, and whether the function of the sphincter of Oddi is normal.

Controversy of CGPC

Even though LC has become a standard for the treatment of cholecystolithiasis, in response to the clinical needs of a large number of patients, China has developed CGPC as a minimally invasive technique for gallbladder preservation and removal of gallbladder stones, as reported by Zhu *et al*.[29] "The Clinical Guideline for Choledochoscopic Gallbladder-preserving Surgery (2021 edition)" issued by the Endoscopy Specialist Branch of the Chinese Medical Doctor Association points out that CGPC has become another valuable surgical method other than cholecystectomy.[38] However, the "Consensus on the Surgical Management of Benign Gallbladder Diseases (2021 edition)" issued by the Branch of Biliary Surgery of Chinese Surgical Society of Chinese Medical Association and Committee of Biliary Surgeons of Chinese Medical Doctor Association firmly opposes CGPC because of the high recurrence rate of stones after choledocholithotomy, and the gallbladder preservation after choledocholithot-

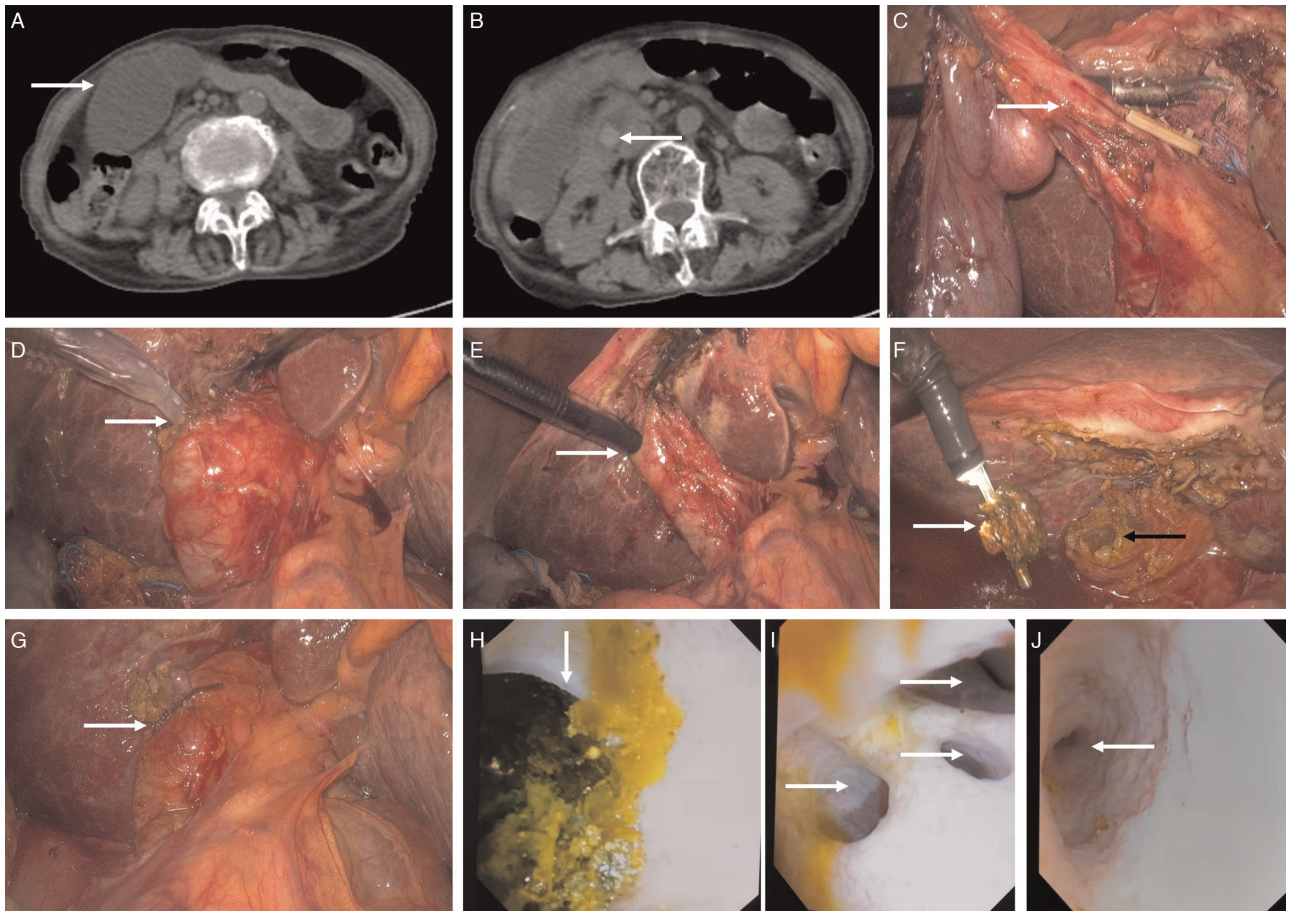

Figure 1: LTCBDE in a 93-year-old female patient with ACC combined with CBD stones. (A) CT showed enlargement and cholestasis of the gallbladder (arrow). (B) CT showed a stone (arrow) in the CBD. (C) Cystic duct of gallbladder (arrow). (D) A catheter (arrow) was inserted through the cystic duct for flushing; (E) Choledochoscope (arrow) was inserted through the cystic duct. (F) The stone (white arrow) was removed from the CBD through the choledochoscopic stone removal basket, the opening of cystic duct stump (black arrow). (G) Ligation (arrow) of cystic duct stump. (H) Stone (arrow) in the CBD. (I) The three opening of right hepatic duct branches (arrows). (J) Proximal opening (arrow) of the CBD. ACC: Acute calculous cholecystitis; CBD: Common bile duct; CT: Computed tomography; LTCBDE: Laparoscopic transcystic common bile duct exploration.

omy is a high-risk factor for gallbladder cancer.[39] The gallbladder preservation and gallbladder resection for cholecystolithiasis is not an innovative technology. Therefore, CGPC still has many clinical problems to be solved, and it cannot be used as the mainstream treatment for cholecystolithiasis.

Merits and demerits of Da Vinci surgical system

In 2000, the Da Vinci robot-assisted surgery system was approved by the United States Food and Drug Administration to enter the clinic. There have been many surgical systems, among which the Da Vinci system is the latest and most widely used. Compared with traditional laparoscopic surgery, the Da Vinci system has a stable freedom mechanical arm with high degree and high-definition three-dimensional (3D) lens, which can carry out flexible and fine surgical procedures in a confined space. Zhang *et al*[40] reported that minimally invasive surgery for malignant biliary diseases was safe and feasible when assisted by the Da Vinci system, and there was a potential advantage in the procedures that required endoscopic reconstruction of the biliary tract. Tang *et al*[41] reported that the Da Vinci system used for radical surgery of perihilar cholangiocarcinoma is feasible, which needs evaluation of long-term prognosis of a large sample size and high-quality clinical research. However, the Da Vinci system also has some disadvantages: lack of tactile feedback (the operator has no tactile perception of the tissues and organs in the surgical field and cannot judge the elasticity, pulsatility, hardness, and toughness of blood vessels, tumors, and other tissues through tactile touch; so, it is particularly unfavorable for the radical surgery of some complex tumors); the price is higher than that of traditional laparoscopic surgery (high purchase, operation, and maintenance costs); and the system technology is complex (the probability of machine failure during the operation is greater than that of general endoscopic surgery systems). The former mentioned "Consensus on the Surgical Management of Benign Gallbladder Diseases (2021 edition)" points out that robotic cholecystectomy is not recommended at present.[39]

Precise technological progress in geriatric biliary surgery

With the great progress of humanistic medicine and evidence-based medicine in the new century, the precise hepatobiliary surgery has become a new concept and technique based on the highly developed biomedical and information science and technology.[42] The development

of visual, quantifiable and controllable precise hepatobiliary surgery has been achieved through 3D visualization, 3D printing, mixed-reality display, indocyanine green (ICG) fluorescence imaging, and other modern technologies, so as to pursue complete clearance of the disease, ensure the structural integrity of the residual hepatobiliary system and the maximum hepatic functional volume, and to maximize the control of intra-operative bleeding and systemic traumatic invasion.

3D visualization

3D visualization is based on computer image processing to analyze, integrate, calculate, segment, and render the imaging data of enhanced CT or enhanced MRI and reconstruct the shape, distribution, course, and spatial structure of the lesion, so as to establish a 3D visualization model. The aim of 3D visualization is to more intuitively, stereoscopically, and accurately display the range of important blood vessels around the tumor and variation in the blood vessels. Therefore, 3D visualization plays an important role in accurately judging the lesion location before surgery, evaluating the relationship between tumor and blood vessels, and formulating a surgical plan. Zeng *et al*[43] reported the data of 32 patients with hilar cholangiocarcinoma and found that liver 3D visualization clearly showed the intrahepatic duct, size and location of tumors, and the relationship between the tumor and intrahepatic pipeline. They concluded that 3D visualization is valuable for optimizing the surgical plan preoperatively and navigating surgery accurately intraoperatively in real time, which may improve the precision of the operation and achieve better recovery. Yang *et al*[44] believe that 3D visualization realizes the combination of individualized medicine, precision medicine, and clinical practice and provides new ideas and methods for the diagnosis and treatment of intrahepatic bile duct stones. However, in addition to the automatic segmentation of software, sometimes manual segmentation is needed to assist in the production of 3D visualization models. Therefore, it is necessary to standardize the recognizability of original data and the proportion of manual segmentation optimization. At the same time, it is possible to realize high-standard 3D visualization processing by following the homogenization processing and quality control system standards, so as to comprehensively evaluate the disease and determine the next treatment plan.

3D printing

3D printing converts 2D image data into 3D model data through computer software and then prints it into a 3D structure layer by layer with specific materials. With the advent of 3D printing technology, images based on 3D reconstruction are quickly transformed into a real model. The model realizes the transformation from the 3D visual image that can only be viewed on the computer screen to the 3D physical model, which is convenient for multidirectional and multiangle observation of diseases during surgery. A 3D physical model can make the surgical plan more accurate, and the site of focus can be located when the anatomical spatial relationship changes during the operation. Yang *et al*[45] reported 15 patients with hilar cholangiocarcinoma with a diagnostic accuracy of 93.3% for Bismuth–Corlette type by 3D visualization and 3D printing models, suggesting that 3D visualization and printing can accurately show the tumor and its associations with the surrounding bile duct, and it can be used to improve the success rate of the operation. It should be pointed out that there are many kinds of 3D printing materials, such as plastics, photosensitive resins, hydrogels, and silica gel. The manufacturing cost between different materials is different, which also has some influence on the speed and fineness of the models. At present, 3D printing technology still has few clinical applications, which may be related to its high cost and complex technology. In addition, there is no unified specification and standard for the objective evaluation of clinical applications, which needs to be further studied in combination with relevant guidelines and clinical practice.

Mixed reality

Mixed reality is a computer technology that enables the display and interaction of virtual 3D reconstructed images in the real environment. The virtual model is generated through computer visual graphics technology and superimposed the images into the real environment which was viewed by users, bringing a mixed scene of reality and virtual reality. The application of the mixed reality technology can combine virtual reality and augmented reality so that the operator can see the image of the real operation area and interact with it through the virtual image, breaking the barrier between the virtual and real worlds, which is convenient for pre-operative planning, surgical simulation, and intra-operative operation.[46] Liu *et al*[47] reported a patient with duodenal tumor and used mixed reality navigate the surgical approach and important anatomical structures, and they successfully completed laparoscopic pancreaticoduodenectomy, indicating that this technology can accurately reconstruct and locate the anatomical structure of the surgical site. Hou and Zhang[48] believe that this technology is a further upgrade of visual presentation technology based on 3D visualization, which helps to improve spatial perception of liver anatomy. Mixed reality is important for pre-operative evaluation and formulation of the surgical plan, accurate and real-time navigation during the operation, and for improving the safety and accuracy of the operation, and is expected to become a new generation of auxiliary tools for hepatobiliary surgery. However, there are still unsolved theoretical problems and technical difficulties for mixed reality technology. For example, under the influence of respiratory movement, operation changes, and surgical instruments, the real-time and accuracy of registration tracking technology and display technology still need to be improved.

ICG fluorescence imaging

ICG fluorescence imaging is a new technology to realize visual operation by using the characteristics that ICG can accumulate in the liver and be captured by near-IR fluorescence imaging. ICG fluorescence imaging technology can define the tumor boundary and detect small or

metastatic lesions at the molecular and cellular levels. Combined with 3D visualization, this technology can more accurately navigate the operation.[49,50] ICG fluorescence cholangiography is safe and efficient and can be operated in real time, which can play an important role in identifying the biliary system and intra-operative bile leakage.[51] The application of ICG fluorescence imaging technology for guiding hepatectomy has a unique application value in identifying tumors, guiding the cutting edge, developing liver segment, and preventing biliary fistula.[52] Wang *et al*[53] reported that this technology was applied to 11 cases of LC and showed that ICG fluorescence cholangiography has a good clinical application value in difficult LC, which can better avoid intra-operative biliary tract injury and reduce intra-operative and post-operative complications. Zhang *et al*[54] reported that this technique was applied to three cases of laparoscopic duodenal-preserving pancreatectomy, which showed that it can effectively prevent bile duct injury and bile leakage. However, ICG fluorescence imaging needs special laparoscopic equipment, which may limit its wide application. Moreover, there are still many problems in the clinical application of ICG, such as the time of pre-operative ICG injection, the influence of the patient's cirrhotic background on ICG clearance, and development characteristics of different tumors, which need to be further discussed and evaluated with a large sample of clinical data.

Peri-operative safety guarantee of older patients with biliary diseases requiring surgery

Older patients with biliary diseases are a high-risk group for surgical treatment. How to ensure their peri-operative safety is a key to improving the therapeutic outcome. Although many studies have pointed out that the damage control concept is conducive to the prevention of peri-operative risks, enhanced recovery after surgery (ERAS) is helpful for peri-operative risk control, and cardiac function monitoring and maintenance are beneficial to avoid peri-operative cardiac accidents, which need to be discussed further to form a broader consensus.

Damage control concept

Older patients with biliary diseases requiring surgery, based on the above mentioned clinical characteristics, have difficulty tolerating long-term anesthesia and complex surgery; therefore, the damage control concept is needed to guide the treatment process. At present, biliary operations that coincide with the damage control concept mainly include percutaneous transhepatic gallbladder drainage (PTGBD), EST, endoscopic nasobiliary drainage, and endoscopic retrograde biliary drainage. It should be emphasized that while mastering the damage control concept, we should also pay attention to the possible hidden dangers of surgery. For example, PTGBD can quickly control and reduce acute gallbladder inflammation, reduce the impact of cholecystectomy on the patient's body, comply with the damage control concept, and is suitable for acute cholecystitis in special situations such as poor general condition, critical conditions, and unstable blood pressure.

Therefore, for patients with high-risk acute suppurative cholecystitis, PTGBD has been included in "Tokyo Guidelines 2018: Management Strategies for Gallbladder Drainage in Patients with Acute Cholecystitis (with videos)" as the preferred surgical treatment.[55] However, there is a lack of sufficient evidence to support the application of PTGBD.[56] Recently, there have been a number of studies to compare percutaneous cholecystostomy (PC, actual PTGBD) with emergency cholecystectomy (EC) for the treatment of ACC in high-risk patients.[57-59] However, the results from these studies varied, making it difficult to reach a consensus.[57] Huang *et al*[58] performed a meta-analysis to compare the efficacy and safety of PC versus EC for the treatment of ACC in high-risk surgical patients. A total of 8960 patients from six studies were finally included. PC resulted in increased risks of mortality and readmission rates as compared with EC. No significant difference was detected between PC and EC in terms of morbidity, severe complication rate, or hospitalization length. Moreover, PC was associated with significantly higher risks of mortality, morbidity, readmission rate, and hospitalization length when directly compared with LC. Therefore, EC is superior to PC for the treatment of ACC in high-risk surgical patients, and LC is the preferred surgical strategy.

Therefore, the application of PTGBD needs to be further evaluated. Our experience is that for older ACC patients with surgical indications, PTGBD should be avoided as far as possible, so as to avoid drainage tube blockage, prolonged hospitalization, increased readmission rate, and even increased mortality. Laparoscopic exploration should be considered as long as patients exclude uncontrollable cardiopulmonary insufficiency. The key to success lies in skilled laparoscopic surgery and strengthening the protection of cardiopulmonary function during the peri-operative period.

For another example, hepatopancreatoduodenectomy (HPD), as one of the methods of extended radical cholecystectomy for advanced gallbladder cancer, has some clinical significance for improving R0 resection rate, prolonging survival time, and improving quality of life despite its trauma. At present, the focus of debate on HPD is its high rate of complications and mortality, with liver failure, pancreatic fistula, and infection being common causes of death. How to reduce the trauma of HPD and achieve the optimal clinical outcomes are still challenging for surgeons.[60-62]

ERAS

ERAS alleviates the stress of surgical trauma and accelerates post-operative recovery after operation and has a positive effect on improving the therapeutic outcome of surgical treatment of biliary diseases in older patients. Wei *et al*[63] retrospectively analyzed the clinical data of 616 patients who underwent elective biliary surgery, with a control group ($n = 312$) receiving traditional peri-operative management, and the ERAS group ($n = 304$). They concluded that application of ERAS and measures in the peri-operative period reduced post-operative pain, accelerated recovery of gastrointestinal function,

promoted post-operative early ambulation, reduced the incidence of post-operative complications, shortened hospital stay, decreased the cost of hospitalization, and enhanced the early recovery of patients.

The "Clinical Practice Guidelines for ERAS in China (2021)," newly released by the Chinese Society of Surgery and Chinese Society of Anesthesiology, points out that with the popularization of precision and minimally invasive technology, ERAS has been more widely used in hepatobiliary surgery.[64] Clinical practice shows that the peri-operative implementation of ERAS in hepatobiliary surgery is safe and effective. ERAS promotes the cooperation of multidisciplinary teams, improves the safety of hepatobiliary surgery, and significantly improves the quality and speed of rehabilitation. However, due to the complexity of biliary diseases requiring surgery in older patients, the operation is difficult and risky. Therefore, during the implementation of the guidelines, an individualized plan should be formulated according to the patient's condition and the technical conditions of the medical institutions and biliary surgeons so that ERAS can ensure safety to the greatest extent.

Cardiac function monitoring and maintenance

Studies have suggested that major adverse cardiac events (MACEs) in older patients with biliary diseases requiring surgery are the main cause of peri-operative accidental death.[65-67] Therefore, timely monitoring and effective maintenance of peri-operative cardiac function stability are important to avoid the occurrence and development of MACEs.[13]

Peri-operative cardiac function monitoring of older patients is mainly realized through intra-operative and post-operative electrocardiography and blood pressure and central venous pressure (CVP) monitoring. Intra-operative blood pressure should be kept stable to prevent large-scale fluctuation. The fluctuation range should be controlled within 20% of basic blood pressure and no more than 30%. Continuous non-invasive arterial blood pressure monitoring provides real-time and continuous waveform data to guide the use of vasoactive drugs during surgery and causes no trauma and few complications. This has attracted more clinical attention in recent years,[68] but its accuracy, particularly in older patients, is still controversial. Intraoperative CVP monitoring is helpful to evaluate myocardial perfusion and cardiac load and to maintain intraoperative hemodynamic stability. Post-operative cardiac function monitoring is helpful to guide the amount and speed of post-operative infusion and prevent heart failure caused by excessive and rapid infusion. Once the signs of myocardial infarction are found, thrombolysis, anticoagulation, and lipid-lowering and symptomatic treatment should be carried out immediately, and percutaneous coronary intervention should be performed when necessary.

We recently reported the clinical data of 372 older patients with biliary diseases and concluded that although the surgical risk was significantly higher than that of the middle-to-low age group, there was no significant difference in the effect of surgical treatment. The key is to focus on maintaining cardiopulmonary function during the peri-operative period so as to effectively improve the surgical outcome and peri-operative safety in older patients with biliary diseases.[65]

In conclusion, it is of great significance to fully understand the focus of controversy, actively make use of its favorable factors, and effectively avoid its unfavorable factors, for further improving the therapeutic effects of geriatric biliary surgical diseases, and thus benefit the vast older patients with biliary surgical diseases.

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Conflicts of interest

None.

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