Observational Study

Medicine®

OPEN

Protective and therapeutic experience of perioperative safety in extremely elderly patients with biliary diseases

Zongming Zhang, MD, PhD*, Yue Zhao, MD, Fangcai Lin, MD, Limin Liu, MD, Chong Zhang, MD, PhD, Zhuo Liu, MD, Mingwen Zhu, MD, Baijiang Wan, MB, Hai Deng, MB, Haiyan Yang, MB, Lijun Jiao, MS, Xiyuan Xie, MS

Abstract

To explore the protective and therapeutic measures of improving perioperative safety in extremely elderly patients with biliary diseases, so as to improve the therapeutic efficacy of surgery.

A retrospective case–control study of 412 elderly patients with biliary diseases was carried out from July 2013 to July 2019. Seventy eight cases were divided into the high age (HA) group (≥80 years) and 334 into the middle–low age (MLA) group (60–79 years).

In the HA compared with MLA group,

1. Preoperative coexisting diseases: the occurrence of coexisting coronary heart disease (CHD), hypertension, chronic bronchitis with emphysema, hypoproteinemia, and anemia were significantly increased;
2. Laboratory examinations: function of liver, kidneys, heart, lungs, and blood coagulation significantly declined;
3. Surgical procedures: open cholecystectomy with transcystic common bile duct (CBD) exploration significantly higher, while laparoscopic cholecystectomy significantly lower;
4. Operative effects: intraoperative blood loss, operation time, postoperative hospital stay, and length of hospitalization significantly increased or prolonged;
5. Postoperative complications: postoperative respiratory failure, pulmonary infection, anemia and electrolyte disorder significantly increased;
6. Therapeutic outcomes: no significant difference in the therapeutic effects.

Although the surgical risk was significantly increased, there was no significant difference in the therapeutic efficacy in the HA compared with MLA group, suggesting that surgical treatment in extremely elderly patients with biliary diseases is safe and feasible. The key is to actively treat preoperative coexisting diseases, strictly adhere to surgical indications, reasonably select surgical procedures, precisely perform the operation, closely monitor and control intraoperative emergencies, timely prevent and treat postoperative complications, so as to improve the perioperative safety of extremely elderly patients with biliary diseases.

Abbreviations: CBD = common bile duct, CHD = coronary heart disease, HA = high age, LC = laparoscopic cholecystectomy, MLA = middle–low age, OTCBDE = open transcystic common bile duct exploration.

Keywords: biliary diseases, extremely elderly patients, perioperative period, safety

Editor: Leonidas G. Koniaris.

Supported by Beijing Municipal Science & Technology Commission (No. Z171100000417056), and the Science and Technology Project of State Grid Corporation of China (No. SGHB0000AJJS1400182).

The authors have no conflicts of interests to disclose.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Department of General Surgery, Beijing Electric Power Hospital, State Grid Corporation of China, Capital Medical University, Beijing, PR China.

** Correspondence: Zongming Zhang, Department of General Surgery, Beijing Electric Power Hospital, State Grid Corporation of China, Capital Medical University, Beijing 100073, PR China (e-mail: zhangzongming@mail.tsinghua.edu.cn).*

How to cite this article: Zhang Z, Zhao Y, Lin F, Liu L, Zhang C, Liu Z, Zhu M, Wan B, Deng H, Yang H, Jiao L, Xie X. Protective and therapeutic experience of perioperative safety in extremely elderly patients with biliary diseases. Medicine 2021;100:21(e26159).

Received: 21 February 2020 / Received in final form: 17 October 2020 / Accepted: 6 May 2021

http://dx.doi.org/10.1097/MD.0000000000026159

1. Introduction

According to the up-to-date information released by the Chinese National Bureau of Statistics, by the end of 2019, the population aged ≥60 years in China reached 253,880,000, accounting for 18.1% of the total population. With the increase in the aging population, biliary diseases, mainly stones, inflammation and tumors have become frequent in China,[1] with a morbidity rate of 8% to 11%.[2] Due to the decline in stress response, defense ability and immunity, elderly patients with biliary diseases have many clinical characteristics, such as multiple coexisting diseases, rapid progression, poor surgical tolerance, high surgical risk, frequent postoperative complications, and high mortality.[3] Extremely elderly patients with biliary diseases are a high-risk population for surgical treatment.[4] How to ensure the perioperative safety in extremely elderly patients who really need surgical treatment is an exasperating problem.[5,6] The present study explored the protective and therapeutic measures of improving perioperative safety in extremely elderly patients with biliary diseases, to strengthen assurance of perioperative safety, and improve the therapeutic efficacy of surgical operation.

2. Material and methods

2.1. Clinical data

2.1.1. General information. This was a retrospective case–control study of 412 elderly patients with biliary diseases treated by the Department of General Surgery, Beijing Electric Power Hospital, State Grid Corporation of China, Capital Medical University between July 2013 and July 2019. According to age, 78 cases were divided into the high age (HA) group (≥ 80 years) and 334 into the medium–low age (MLA) group (60–79 years).

2.1.2. Inclusion and exclusion criteria. Inclusion criteria:

1. age ≥60 years;
2. definite diagnosis of biliary diseases;
3. clear operative indications;
4. patients and their families agreed to surgical treatment, and gave signed informed consent.

Exclusion criteria:

1. age <60 years;
2. uncontrollable cardiopulmonary insufficiency; and
3. patients or their families refused surgical treatment.

The study was approved by the Ethics Committee of Beijing Electric Power Hospital, State Grid Corporation of China, with the approval number of KY-2018-101-01-X.

2.1.3. Laboratory and imaging examinations. Before surgery, function of liver, kidneys, heart, lungs and coagulation system was routinely examined. When necessary, echocardiography, 24-hours dynamic electrocardiography (ECG), coronary artery computed tomography angiography (CTA), craniocerebral magnetic resonance angiography (MRA), and head and neck CTA, were carried out to examine the function of important organs. At the same time, abdominal B ultrasound, CT, magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP) were performed to confirm the exact diagnosis of biliary diseases.

2.1.4. Surgical procedures. According to the individual patient's status, an appropriate surgical procedure was selected. For elderly patients with benign biliary diseases, it was reasonable to select laparoscopic cholecystectomy (LC), laparoscopic transcystic common bile duct exploration, laparoscopic common bile duct exploration with T-tube drainage (LCBDE+T), open cholecystectomy, open transcystic common bile duct exploration (OTCBDE), open common bile duct exploration with T-tube drainage (OCBDE+T), hepatolobectomy, LC+endoscopic sphincterotomy (EST) or endoscopic papillary balloon dilatation (EPBD) via laparoscopy combined with homochronous endoscopy or choledochoscopy. For elderly patients with malignant biliary diseases, radical pancreaticoduodenectomy, radical resection of hilar cholangiocarcinoma, radical resection of gallbladder cancer, palliative modified loop cholecystojejunostomy and gastrojejunostomy with Braun anastomosis, was selected.

2.1.5. Follow-up. Follow-up was conducted by outpatient visit and telephone. The elderly patients with benign biliary diseases were questioned about the occurrence of delayed bile duct injury and postoperative recurrence or regeneration of common bile duct (CBD) stones, and whether postoperative tumor recurrence occurred in elderly patients with malignant biliary diseases.

2.1.6. Statistical analysis. SPSS version 22.0 was used for statistical analysis. The measurement data were expressed as mean ± SD. If normal distribution was satisfied, Student *t* test was used for comparison between 2 independent samples. When the variance was uneven, the corrected *t*-test was used. If there was no normal distribution, the data were expressed by the median and quartile spacing (P25–P75) and compared by Mann–Whitney *U* rank sum test. The enumeration data were expressed as rate (%) or constituent ratio, and the χ^2 test was used for comparisons between 2 groups. Continuity correction or Fisher exact probability test was used for results that did not satisfy the conditions. The rank data were tested by Mann–Whitney *U* rank sum test for comparisons between 2 independent samples. The Kaplan–Meier method was used to calculate survival time and draw the survival curve. $P < .05$ was considered statistically significant.

3. Results

3.1. Age

The age distribution of 412 elderly patients with biliary diseases was 60 to 96 years, with an average of 71.9 ± 8.6 years. In the HA group, the average age of 69 patients was 84.4 ± 3.9 years, ranging from 80 to 96 years. In the MLA group, the average age was 68.3 ± 5.8 years, ranging from 60 to 79 years.

3.2. Types of biliary diseases

The 3 most common biliary diseases were cholecystolithiasis, acute cholecystitis and choledocholithiasis. Among them, 143 (34.7%) patients had 1 type of biliary disease, 210 (51.0%) had 2 types, and 59 (14.3%) had 3 types. The distribution of types of diseases in the HA compared with MLA group is shown in Table 1. There was no significant difference in the distribution of disease types between the 2 groups, except CBD stones.

3.3. Preoperative coexisting diseases

There were 11 preoperative coexisting diseases, such as coronary heart disease (CHD), hypertension and diabetes mellitus, and 344

Table 1

Distribution of disease type in HA and MLA groups, n (%).

Type of disease	HA group	MLA group	χ^2/Fisher	*P* value
Gallbladder stones	51 (33.1)	229 (39.1)	0.293	>.05*
CBD stones	30 (19.5)	87 (14.8)	4.792	<.05*
Hepatolithiasis	1 (0.7)	3 (0.5)	-	>.05†
Chronic cholecystitis	3 (2.0)	36 (6.1)	3.546	>.05*
Acute cholecystitis	47 (30.5)	168 (28.7)	2.512	>.05*
Gallbladder polyps	2 (1.3)	13 (2.2)	0.052	>.05*
Acute cholangitis	9 (5.8)	17 (2.9)	3.424	>.05*
Biliary pancreatitis	6 (3.9)	10 (1.7)	2.587	>.05*
Biliary tract tumors	5 (3.2)	15 (2.6)	0.174	>.05*
Gallbladder carcinoma	0 (0.0)	8 (1.4)	0.855	>.05*
Total	154 (100)	586 (100)		

A single patient may have 1 to 3 types of biliary diseases.
* χ^2 test.
† Fisher exact probability test.

(83.5%) patients had at least 1 coexisting disease. In the HA group, patients had 0 to 8 preoperative coexisting diseases: 2 (2.6%) had no coexisting diseases, 18 (23.1%) had 1, and 13 (16.7%) had 2. In the MLA group, patients had 0 to 6 preoperative coexisting diseases, 66 (19.8%) had no coexisting diseases, 85 (25.4%) had 1, and 89 (26.6%) had 2. The proportion of preoperative coexisting CHD, hypertension, chronic bronchitis with emphysema, hypoproteinemia, and anemia were significantly increased, instead of diabetes mellitus was significant decreased in the HA compared with MLA group ($P < .05$) (Table 2).

3.4. Laboratory examinations

Preoperative white blood cell count, neutrophil percentage, high-sensitivity C-reactive protein (Hs-CRP), aspartate aminotransferas (AST), total bilirubin (TBil), direct bilirubin (DBil), creatinine, brain natriuretic pepttide (BNP), high-sensitivity troponin I (HsTn-I), myoglobin, prothrombin time (PT), international normalized ratio (INR), fibrinogen (Fib), D-dimer (D-D) in blood were significantly increased, whereas hemoglobin (Hb), total protein (TP) and albumin (Alb) were significantly decreased, in the HA compared with MLA group ($P < .05$) (Table 3). This suggested that the preoperative function of liver, kidneys, heart, lungs and blood coagulation in the HA group were significantly lower compared with those in the MLA group.

3.5. Surgical procedures

Four hundred twelve patients underwent surgical treatment with one of 12 procedures (Table 4), including pancreaticoduodenectomy, radical resection of hilar cholangiocarcinoma, or radical resection of gallbladder carcinoma. The number of patients who underwent OC+OTCBDE was significantly higher, while the number who underwent LC was significantly lower, in the HA compared with MLA group ($P < .05$).

3.6. Operative effects

The intraoperative blood loss, operating time, postoperative hospital stay, and length of hospitalization were significantly increased or prolonged ($P < .05$) in the HA compared with MLA group (Table 5).

3.7. Postoperative complications

Ten postoperative complications were recorded: hypoproteinemia, electrolyte disorder, incision fat liquefaction, respiratory failure, hepatic insufficiency, renal insufficiency, pulmonary infection, heart failure or myocardial infarction, anemia, biliary or pancreatic fistula. Hypoproteinemia had the highest incidence, followed by anemia and electrolyte disturbance. A single patient could have 1 to 6 postoperative complications. The number of patients with postoperative respiratory failure, pulmonary

Table 2

Comparison of distribution of coexisting diseases in HA and MLA groups, n (%).

Type of coexisting disease	HA group	MLA group	χ^2	*P* value
Coronary heart disease	26 (33.3)	59 (17.7)	9.481	<.05
Hypertension	52 (66.7)	159 (47.6)	9.196	<.05
Diabetes mellitus	8 (10.3)	79 (23.7)	6.812	<.05
Old cerebral infarction	18 (23.1)	50 (15.0)	3.016	>.05
Chronic bronchitis and emphysema	12 (15.4)	11 (3.3)	15.320	<.05
Pulmonary infection	4 (5.1)	6 (1.8)	1.724	>.05
Hepatic insufficiency	28 (35.9)	92 (27.5)	2.137	>.05
Renal insufficiency	4 (5.1)	12 (3.6)	0.094	>.05
Electrolyte disorder	10 (12.8)	24 (7.2)	2.652	>.05
Hypoproteinemia	30 (38.5)	85 (25.4)	5.321	<.05
Anemia	30 (38.5)	39 (11.7)	32.537	<.05

Table 3

Comparison of laboratory test results before operation in HA and MLA groups [M (P_{25}-P_{75})].

Item	HA group	MLA group	Z	*P* value
Blood routine				
WBC ($\times10^9$/L)	8.5 (5.8–13.0)	6.7 (5.3–10.5)	−2.726	<.05
N (%)	83.8 (71.1–89.5)	72.9 (61.3–86.2)	−3.790	<.05
Hb (g/L)	119.5 (104.0–138.3)	130.0 (120.0–139.0)	−3.545	<.05
Blood biochemistry				
Hs-CRP (mg/L)	62.3 (7.2–115.3)	12.6 (1.8–69.7)	−4.073	<.05
ALT (U/L)	37.0 (14.0–114.0)	25.0 (14.0–98.3)	−0.565	>.05
AST (U/L)	36.5 (19.0–112.3)	23.0 (17.0–77.0)	−2.158	<.05
TP (g/L)	61.0 (56.0–65.8)	65.1 (60.2–69.7)	−3.646	<.05
Alb (g/L)	34.5 (31.3–38.1)	38.5 (35.0–42.2)	−5.516	<.05
TBil (μmol/L)	28.2 (14.1–67.8)	18.6 (12.0–34.0)	−2.781	<.05
DBil (μmol/L)	8.4 (3.6–39.8)	4.1 (2.5–13.6)	−3.604	<.05
Cr (μmol/L)	83.0 (69.3–97.3)	72.0 (61.8–85.0)	−3.718	<.05
Glu (mmol/L)	5.9 (5.0–7.4)	6.1 (5.0–7.8)	−1.264	>.05
Cardiac index				
BNP (pg/mL)	85.9 (55.8–251.4)	66.0 (31.8–116.0)	−2.789	<.05
HsTn-I ($\times10^{-2}$ng/mL)	0.7 (0.4–1.5)	0.4 (0.2–0.7)	−3.733	<.05
CKMB (ng/mL)	1.0 (0.5–1.6)	0.8 (0.5–1.2)	−1.572	>.05
Myo (ng/ml)	71.5 (40.8–108.5)	44.7 (32.1–69.0)	−2.900	<.05
Blood coagulation function				
APTT (s)	32.0 (30.0–35.0)	31.7 (29.5–34.1)	−1.238	>.05
PT (s)	11.7 (10.8–12.7)	11.2 (10.6–12.3)	−2.631	<.05
INR	1.1 (1.0–1.2)	1.0 (1.0–1.1)	−2.965	<.05
Fib (g/L)	3.9 (3.2–4.7)	3.5 (2.8–4.3)	−2.887	<.05
D-D (mg/L)	0.4 (0.2–0.8)	0.2 (0.1–0.5)	−4.465	<.05

Alb = albumin, ALT = alanine aminotransferase, APTT = activated partial thromboplastin time, AST = aspartate aminotransferas, BNP = B-type natriuretic peptide, CKMB = creatine kinase isoenzyme, Cr = creatinine, DBil = direct bilirubin, D-D = D-dimer, Fib = fibrinogen, Glu = glucose, Hb = hemoglobin, Hs-CRP = high sensitivity C-reactive protein, HsTn-I = high-sensitivity troponin I, INR = international normalized ratio, MYO = myoglobin, N = neutrophil percentage, PT = prothrombin time, TBil = total bilirubin, TP = total protein, WBC = white blood cell count.

infection, anemia and electrolyte disorder was significantly increased in the HA compared with MLA group ($P<.05$) (Table 6).

3.8. Therapeutic outcomes

Among 412 elderly patients, 402 (97.6%) were cured, 2 (0.5%) improved, and 8 (1.9%) died. In the HA group, 75 patients were cured, with a cure rate of 96.2% (75/78), 1 (1.3%) improved, and 2 (2.5%) patients died of acute myocardial infarction at 2 and 4 days after surgery, respectively. In the MLA group, 327 patients were cured, with a cure rate of 97.9% (327/334), 1 (0.3%) improved, and 6 (1.8%) patients died at 6, 7, 14, 18, 18, and 31 days after surgery, with 1 who died due to acute pulmonary embolism, 1 acute heart failure, 1 acute myocardial infarction, 1 acute cerebral infarction, and 2 multiple organ failure. No

Table 4

Comparison of surgical procedures in HA and MLA groups, n (%).

Surgical procedure	HA group	MLA group	χ^2/ Fisher	*P* value
Pancreaticoduodenectomy	2 (2.6)	8 (2.4)	0.000	>.05*
Radical resection of hilar cholangiocarcinoma	2 (2.6)	4 (1.2)	0.146	>.05*
Radical resection of gallbladder carcinoma	0 (0.0)	6 (1.8)	0.446	>.05*
Hepatolobectomy	1 (1.3)	3 (0.9)	–	>.05†
OC	5 (6.4)	10 (3.0)	1.242	>.05*
OC+OTCBDE	12 (15.4)	21 (6.3)	7.102	<.05*
OC+OCBDE+T	8 (10.3)	14 (4.2)	3.480	>.05*
LC	35 (44.9)	217 (65.0)	10.753	<.05*
LC+LTCBDE	7 (9.0)	18 (5.4)	0.866	>.05*
LC+LCBDE+T	4 (5.1)	23 (6.9)	0.319	>.05*
LC + EST / EPBD	0 (0.0)	7 (2.1)	0.645	>.05*
PMLCG	2 (2.6)	3 (0.9)		>.05†

* χ^2 test.

† Fisher exact probability test.

EPBD = ndoscopic papillary balloon dilatation, EST = endoscopic sphincterotomy, LC = laparoscopic cholecystectomy, LCBDE+T = laparoscopic common bile duct exploration with T-tube drainage, LTCBDE = laparoscopic transcystic common bile duct exploration, OC = open cholecystectomy, OCBDE+T = open common bile duct exploration with T-tube drainage, OTCBDE = open transcystic common bile duct exploration, PMLCG = palliative modified loop cholecystojejunostomy and gastrojejunostomy with Braun's anastomosis.

Table 5

Comparison of operative effects in HA and MLA groups [M (P_{25}-P_{75})].

Item	HA group	MLA group	Z	*P* value
The intraoperative blood loss (ml)	30.0 (20.0–100)	15.0 (10.0–30.0)	−4.275	<.05
Operation time (min)	92.5 (70.0–141.3)	75.0 (50.0–115.0)	−3.227	<.05
Postoperative hospital stay (d)	10.0 (6.0–16.5)	7.0 (4.0–11.0)	−3.752	<.05
Length of hospitalization (d)	17.0 (11.8–23.0)	13.0 (9.0–19.0)	−3.368	<.05

Table 6

Comparison of postoperative complications in HA and MLA groups, n (%).

Complication	HA group	MLA group	χ^2	*P* value
Hypoproteinemia	31 (39.7)	104 (31.1)	2.126	>.05
Electrolyte disorder	17 (21.8)	43 (12.9)	4.044	<.05
Incision fat liquefaction	1 (1.3)	7 (2.1)	0.000	>.05
Respiratory failure	6 (7.7)	1 (0.3)	16.503	<.05
Hepatic insufficiency,	2 (2.6)	16 (4.8)	0.312	>.05
Renal insufficiency	5 (6.4)	7 (2.1)	2.777	>.05
Pulmonary infection	12 (15.4)	10 (3.0)	16.833	<.05
Heart failure or myocardial infarction	3 (3.8)	9 (2.7)	0.029	>.05
Anemia	28 (35.9)	78 (23.4)	5.207	<.05
Biliary or pancreatic fistula	2 (2.6)	8 (2.4)	0.000	>.05

A single patient may have 1 to 6 kinds of postoperative complications.

Table 7

Comparison of therapeutic effects in HA and MLA groups, n (%).

Therapeutic effects	HA group	MLA group	Z	*P* value
Cured	75 (96.2%)	327 (97.9%)		
Improved	1 (1.3%)	1 (0.3%)		
Died	2 (2.5%)	6 (1.8%)		
Total	78	334	−0.895	>.05

significant difference in the therapeutic effects between the 2 groups was observed using the Mann–Whitney *U* rank sum test ($P > .05$) (Table 7).

3.9. Follow-up

The follow-up time was up to July 31, 2020. Among the 412 patients, 397 underwent follow-up, with a follow-up rate of 96.4%. Three hundred seventy one patients with benign biliary diseases were followed up and thirteen were lost. No patients had delayed bile duct injury, or recurrence or regeneration of CBD stones. Twenty six patients with malignant biliary diseases were followed up and 2 were lost. There was only 1 case of tumor recurrence (3 years after radical surgery for T3 gallbladder cancer). The survival time was 0.5 to 77.7 months. The average survival time was 23.5 ± 5.5 months. The median survival time was 12.3 months with the 95% confidence interval of 4.9 to 19.7 months. The overall survival curve was shown in Figure 1.

4. Discussion

4.1. Actively manage preoperative coexisting diseases

In elderly patients with biliary diseases, the morbidity of preoperative coexisting diseases was as high as 65% to 90%, and often combined with one or more coexisting diseases.[3] In particular, in elderly patients with cholelithiasis, the morbidity was as high as 30% and increased with age, and the incidence of coexisting diseases was 47.8%, including 13.7% with 2 or 3 diseases.[7]

We found 11 preoperative coexisting diseases such as CHD, hypertension and diabetes mellitus, and 344 (83.5%) patients had at least 1 coexisting disease. Compared with the MLA group, the number of patients with preoperative coexisting CHD, hypertension, chronic bronchitis with emphysema, hypoproteinemia, and anemia in the HA group was significantly increased. This indicated that active treatment of preoperative coexisting diseases is a key factor to ensure perioperative safety of elderly patients.

For elderly patients with coexisting CHD, if cardiac dysfunction or arrhythmia can be controlled by drugs, cardiac compensatory function is better, and ejection fraction is >60%, surgical treatment can be considered.[8] If patients have a history of cardiac dysfunction, surgery can only be performed when the illness has been stable for 1 month. If patients have a history of AMI, surgery should only be performed when the illness has been stable for at least 6 months. In patients with symptoms of AMI, the serum levels of BNP, cTnI, creatine kinase MB (CKMB) and myoglobin should be measured urgently to establish the severity of heart failure and myocardial injury. If the levels of cTnI, CKMB and myoglobin are increased, suggesting diagnosis of AMI, which should be actively treated, the operation

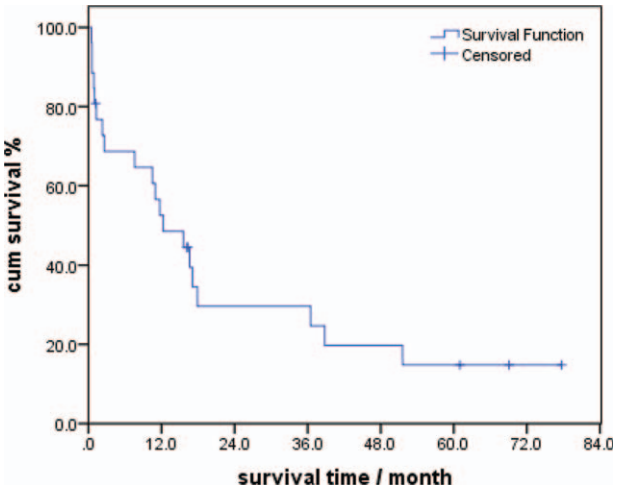

Figure 1. Overall survival curve of 26 elderly patients with malignant biliary tumors after surgery.

should be undertaken carefully or postponed. If patients have a history of bradycardia, a cardiac pacemaker should be implanted before surgery.

For elderly patients with coexisting hypertension, it is suggested that thiazide diuretics, calcium channel blockers, β−receptor blockers and other antihypertensive drugs[9] should be taken before the operation, so that preoperative blood pressure is maintained below 140/90 mm Hg. Some researchers have also suggested that preoperative blood pressure should be below 135/85 mm Hg, and remain stable for 1 to 2 weeks. It is noteworthy that if patients take drugsthat cause intractable hypotension during the perioperative period for a long time, such as reserpine, compound anti-hypertensive tablets (No. 0) and pargyline (monoamine oxidase inhibitor), in the case of non-emergency surgery, these drugs should be ceased and switched to other anti-hypertensive drugs 7 days prior to surgery, so as to avoid catecholamine depletion in the peripheral sympathetic nerve endings, which makes it difficult to improve and maintain blood pressure when hypotension occurs during surgery.

4.2. Strictly adhere to surgical indications

In elderly patients with biliary diseases, it is necessary to adhere strictly to the surgical indications based on their characteristics of coexisting diseases, rapid progression, poor tolerance, higher risk and more postoperative complications.

For elderly patients with common and multiple cholecystolithiasis, surgery can be determined based on the size of stones, gallbladder function, history of biliary colic, and whether the disease is complicated by cholangitis or pancreatitis. Surgery should be performed as soon as possible to avoid increased surgical risk due to increased age, disease progression and other coexisting diseases.[10,11]

For elderly patients with acute calculous cholecystitis, based on our own clinical experience[12,13] and domestic and foreign literature, we propose one of the following 6 parameters as operative indications:

1. body temperature ≥38.5°C;
2. peripheral blood leukocyte count $\geq 1.5 \times 10^{10}$/L;
3. neutrophil ratio ≥85%;
4. hs-CRP ≥100 mg/L;
5. B-ultrasonography shows the double layer structure of the gallbladder wall; and
6. CT or MRI shows pericholecystic or perihepatic fluid.

For elderly patients with choledocholithiasis, surgery can be determined based on the size and number of stones, and diameter of the CBD.[14]

For elderly patients with biliary tract tumors, based on the site of obstruction, the degree of invasion and presence of distant metastasis, surgery should be performed as soon as possible.

In the present study, preoperative severe inflammatory reaction, poor nutritional status, liver and kidney function, cardiac function and coagulation function were compared between the HA and MLA groups. There were no significant differences in the therapeutic effects between the 2 groups, indicating that strict adherence to the surgical indications can reduce the surgical risk.

4.3. Reasonably select surgical procedures

It is important for biliary diseases in elderly patients to choose appropriate surgical procedures,[15] not only to avoid the long course of disease after conservative surgery, or even the possibility of secondary operation, but also to avoid radical surgery and increase the risk of operation.

Take acute gangrenous cholecystitis for an example, conservative surgery such as percutaneous cholecystostomy is theoretically suitable for patients in poor general condition, with serious illness, unstable blood pressure during surgery, and other special circumstances.[16,17] However, percutaneous cholecystostomy should be avoided due to the above-mentioned disadvantages of conservative surgery.[18–20] In our present study, none of the patients underwent percutaneous cholecystostomy. Aggressive surgery such as LC should also be selected with caution in patients with poor preoperative heart and pulmonary function, especially in the presence of emphysema. If LC must be performed, intraoperative pneumoperitoneum pressure should be controlled to below 10 mm Hg to reduce the impact of pneumoperitoneum on heart and pulmonary function. As for the upper age limit for patients undergoing LC, there is no clear opinion at present. The oldest patients were a 96-year-old reported by Lee et al[21] and a 102-year-old reported in China.[22] The maximum age of LC patient in our present study was 96 years.

For elderly patients with malignant tumors in the proximal end of the CBD, based on location, size, degree of invasion and presence of distant metastasis, radical pancreaticoduodenectomy is preferred. Otherwise, if the patients are not suitable or cannot tolerate radical surgery, palliative modified loop cholecystojejunostomy and gastrojejunostomy with Braun's anastomosis can also be used, so as to alleviate jaundice, improve diet, prolong life and improve quality of life.[23]

4.4. Precisely perform the operation

Success of LC in elderly patients with biliary diseases depends not only on the severity of local lesions, but also on the laparoscopic skill of the surgeon.[24,25] In our study, the success rate of LC in elderly patients with acute calculous cholecystitis was 100%. The key to success lies in precise operation during LC; use of a suction

device to skillfully separate inflammatory edema and adhesions in the neck of the gallbladder; use of silk thread to ligate or suture the enlarged, thickened and merged sheet-like cystic duct; and if necessary, use of Hem-O-lock or absorbable clamp to reinforce the ligature.

The strategy for modern precision biliary surgery is to maximize resection of the target lesions, protection of the remaining liver, and reduction of surgical trauma.[26] The technical features of precision biliary surgery are fully visible, quantifiable and controllable. Visualization makes the internal physiological structure of the intrahepatic bile duct visible and thus improves the success rate of the operation. Quantifiable techniques can be used to quantify the boundary of the lesion, so as to precisely excise the lesions. Controllable techniques can remove the lesion completely, while protecting the normal tissue, without damage.[27]

4.5. Closely monitor and control intraoperative emergencies

In elderly patients with biliary diseases, intraoperative monitoring of ECG, blood pressure, arterial pressure and central venous pressure should be strengthened. Meanwhile, any changes in urine volume and body temperature should be noted. When necessary, arterial blood gas analysis should be done, and any abnormalities treated timeously, so that patients tolerate surgery safely and recover from the operation successfully.

ECG should be monitored during the operation, along with heart rate and rhythm. If myocardial ischemia occurs, nitroglycerin can be given by nasal or intravenous drip. If heart failure occurs, the inducing factor should be actively removed, and cardiotonic agents and diuretics can be given intravenously. For patients with arrhythmia, if it is sinus bradycardia or atrioventricular junctional arrhythmia, the depth of anesthesia should be reduced and atropine should be injected intravenously; if rapid atrial fibrillation and even atrial flutter occur, cedilanid can be injected intravenously; if ventricular arrhythmia occurs, lidocaine and amiodarone can be given intravenously. In case of cardiac arrest, cardiopulmonary resuscitation and vasoactive drugs should be given immediately.

Blood pressure should be monitored during the operation, so as to maintain blood pressure stability and prevent fluctuation. During the operation, the permissible blood pressure fluctuation is 20% of basal blood pressure, and the maximum should not exceed 30%. If hypotension occurs during the operation, we should establish the causes, judge whether there is insufficient blood volume, too deep anesthesia or insufficient myocardial blood output, perform appropriate treatment, and administer small doses of ephedrine or dopamine and other drugs. If blood pressure is too high during the operation, the depth of anesthesia should be paid more attention, and nitroglycerin or sodium nitroprusside should be given intravenously. Continuous non-invasive arterial pressure (CNAP) can provide real-time and continuous waveforms and data, so as to guide the use of vasoactive drugs. In addition to its non-invasiveness and fewer complications, CNAP has received more clinical attention in recent years.[28,29] However, its accuracy and precision are still controversial.

Intraoperative monitoring of central venous pressure (CVP), arterial blood gas, and urine volume is helpful to assess myocardial perfusion and cardiac load, and maintain intraoperative hemodynamic stability. If patients with heart failure, severe valvular disease, shock, and other conditions with a significant impact on hemodynamics and difficult to correct before surgery, intraoperative use of pulmonary artery catheterization is recommended.

Intraoperative temperature monitoring prevents hypothermia that easily occurs in elderly patients due to serious decline of their temperature regulation. The temperature during operation should be maintained at no less than 36°C through use of a pressure warm blanket, liquid warmer and other equipment.[30]

4.6. Timely prevention and treatment of postoperative complications

Elderly patients with biliary diseases are prone to various postoperative complications because of their poor body resistance, decreased immunity and more preoperative coexisting diseases.

The clinical data in the present study show that hypoproteinemia had the highest incidence, followed by anemia and electrolyte disturbance. The number of patients with postoperative respiratory failure, pulmonary infection, anemia and electrolyte disorder was significantly increased in the HA compared with MLA group, indicating active prevention and treatment should be given.

For postoperative electrolyte disturbance caused by many factors, such as surgical stress reaction, fasting, gastrointestinal decompression, or bile duct drainage, it is necessary to supplement various electrolytes to maintain water, electrolyte and acid–base balance. For postoperative hypokalemia, it is appropriate to detect and actively deal with it timeously, and if necessary, administer micro-pump intravenous infusion.

It is advisable to remove as soon as possible after the operation the nasogastric decompression tube that is often placed in patients undergoing major biliary surgery, in order to avoid excessive stimulation of the pharynx that can cause cough and expectoration.[31] Postoperative analgesia can help patients expel respiratory secretions as soon as possible and reduce pulmonary complications.[32] However, for elderly patients, the dosage of analgesics should be properly controlled to avoid excessive sedation or respiratory depression.

4.7. Strengthening maintenance of cardiopulmonary function during theperioperative period

In elderly patients with biliary diseases, besides strengthening the preoperative and intraoperative monitoring of cardiopulmonary function, the postoperative maintenance of cardiopulmonary function should also be paid more attention. After the operation, ECG monitoring, measurement of CVP and observation of urine volume should be undertaken. If necessary, the volume of urine per hour should be recorded, so as to guide the volume and speed of infusion after the operation, and to prevent heart failure and pulmonary edema caused by excessive and rapid infusion. At the same time, patients should be encouraged to breathe deeply and cough phlegm, change their position regularly, keep the respiratory tract unobstructed, prevent respiratory tract infection, and reduce the incidence of atelectasis and pneumonia.

For patients with CHD, the postoperative serum levels of BNP, cTnI, CKMB, and myoglobin should be examined dynamically, so as to judge whether heart failure and myocardial injury have occurred and their severity.[33–35] Significant increases in serum levels of cTnI, CKMB, and myoglobin are suggestive of AMI,

which should be actively treated by thrombolysis, anticoagulation, lipid-lowering drugs, symptomatic treatment, and even percutaneous coronary intervention.

In order to prevent and control postoperative pulmonary infection, the physical therapy and expectorant drugs should be used to assist expectoration after the operation, such as routine aerosol and oxygen inhalation, early bed or under-bed activities, oral care, sputum bacteria culture and fungal detection. Meanwhile, we should strictly guard against the occurrence of pulmonary infection caused by vomiting and aspiration, which can be caused by a decrease in lower esophageal sphincter tension after surgery. In case of shortness of breath and difficulty in expelling sputum, a ventilator should be used to inhale airway secretions and maintain adequate ventilation as early as possible, and not wait until the emergence of respiratory failure before considering the use of a ventilator.[36]

5. Conclusion

The key factors in improving therapeutic efficacy of surgery in extremely elderly patients with biliary diseases are: active management of preoperative coexisting diseases; strict adherence to the operative indications; selection of appropriate surgical procedures; precisely perform the operation; closely monitor and control intraoperative emergencies; prevention and treatment of postoperative complications; and focusing on maintenance of cardiopulmonary function during the perioperative period.

Author contributions

Conceptualization: Zongming Zhang.
Data curation: Yue Zhao, Limin Liu, Chong Zhang, Xiyuan Xie.
Funding acquisition: Zongming Zhang.
Investigation: Zongming Zhang, Yue Zhao, Zhuo Liu, Mingwen Zhu, Baijiang Wan, Hai Deng, Haiyan Yang.
Software: Yue Zhao, Lijun Jiao, Xiyuan Xie.
Supervision: Fangcai Lin.
Writing – review & editing: Zongming Zhang.

References

[1] Zhang ZM, Zhao Y, Lin FC, Zhang C, Liu Z, Liu LM. Exploration of preventive and therapeutic measures for perioperative safety in the extremely elderly patients with biliary diseases. Chin J Hepatobiliary Surg 2020;26:104–8.
[2] Zhang ZM, Dong JH, Lin FC, Wang QS, Xu Z, He XD. Current status of surgical treatment of biliary diseases in elderly patients in China. Chin Med J 2018;131:1873–6.
[3] Zhang ZM, Liu Z, Liu LM, Zhang C, Yu HW, Wan BJ. Therapeutic experience of 289 elderly patients with biliary diseases. World J Gastroenterol 2017;23:2424–34.
[4] Lord AC, Hicks G, Pearce B, Tanno L, Pucher PH. Safety and outcomes of laparoscopic cholecystectomy in the extremely elderly: a systematic review and meta-analysis. Acta Chir Belg 2019;119:349–56.
[5] Ablett AD, McCarthy K, Carter B, et al. A practical risk scale for predicting morbidity and mortality in the emergency general surgical setting: a prospective multi-center study. Int J Surg 2018;60:236–44.
[6] Park SY, Chung JS, Kim SH, et al. The safety and prognostic factors for mortality in extremely elderly patients undergoing an emergency operation. Surg Today 2016;46:241–7.
[7] Chen X, Zhou SJ, Cai H. Clinical analysis of 1853 elderly patients with cholelithiasis. J Hepatobiliary Surg 2009;17:130–1.
[8] Zhang K. Surgical management of biliary diseases in the elderly. Chinese Community Doctors (Medical Speciality) 2011;13:75.
[9] Lopatowska P, Mlodawska E, Tomaszuk-Kazberuk A, et al. Adhering to the principles of clinical pharmacology - the correct fixed combinations of antihypertensive drugs. Expert Rev Clin Pharmacol 2018;11:165–70.
[10] Zhang ZM, Liu Z, Liu LM, et al. Experience of laparoscopic cholecystectomy in elderly patients with acute calculous cholecystitis. J Abdominal Surg 2017;30:364.
[11] Nishida Y, Otagiri N, Yoshifuku S, et al. Dementia in elderly patients undergoing early cholecystectomy for acute cholecystitis: a retrospective observational study. BMC Surg 2019;19:71.
[12] Zhang ZM, Wei WP, Liu Z, et al. Opportunity of laparoscopic cholecystectomy in elderly patients with acute calculous cholecystitis. Chinese Journal of Operative Procedures of General Surgery (Electronic Edition) 2016;10:406–9.
[13] Zhang ZM, Song MM, Liu Z, Zhang C, Liu LM, Yu HW. Clinical effect and analysis of laparoscopic cholecystectomy in elderly patients with acute calculous cholecystitis. Chinese Journal of Operative Procedures of General Surgery (Electronic Edition) 2016;10:466–8.
[14] Lupinacci RM, Nadal LR, Rego RE, Dias AR, Marcari RS, Lupinacci RA. Surgical management of gallbladder disease in the very elderly: are we operating them at the right time? Eur J Gastroenterol Hepatol 2013;25:380–4.
[15] Qu Q, Chen W, Liu X, Wang W, Hong T, Liu W. Role of gallbladder-preserving surgery in the treatment of gallstone diseases in young and middle-aged patients in China: results of a 10-year prospective study. Surgery 2020;167:283–9.
[16] Reilly C, Dayal S, Ogedegbe C, et al. Percutaneous cholecystostomy tube leading to a "Floating" gallbladder: a case report. Cureus 2019;11: e5034.
[17] Lin D, Wu S, Fan Y, et al. Comparison of laparoscopic cholecystectomy and delayed laparoscopic cholecystectomy in aged acute calculous cholecystitis: a cohort study. Surg Endosc 2020;34:2994–3001.
[18] Bai GW. Exploration of choice of surgical opportunity and methods for in elderly patients with Cholelithiasis. Chin J Trauma Disability Med 2013;21:110–1.
[19] Li YL, Wong KH, Chiu KWH, Cheng AKC, Cheung RKO, Yam MKH. Percutaneous cholecystostomy for high-risk patients with acute cholangitis. Medicine (Baltimore) 2018;97:e0735.
[20] Søreide JA, Fjetland A, Desserud KF, Greve OJ, Fjetland L. Percutaneous cholecystostomy – an option in selected patients with acute cholecystitis. Medicine (Baltimore) 2020;99:e20101.
[21] Lee SI, Na BG, Yoo YS, et al. Clinical outcome for laparoscopic cholecystectomy in extremely elderly patients. Ann Surg Treat Res 2015;88:145–51.
[22] Ru HY, Yin WS, Zhuang SH. Clinical application of laparoscopic cholecystectomy in elderly patients. J Logistics Univers PAPF (Medical Sciences) 2015;24:382–3.
[23] Zhang ZM, Xing HL, Yuan HM, Liu K, Zhu JP, Su YM. Diagnosis and treatment for advanced hilar cholangiocarcinoma: experience of 24 cases. Frontiers Med China 2008;2:134–8.
[24] Pavlidis TE, Marakis GN, Symeonidis N, et al. Considerations concerning laparoscopic cholecystectomy in the extremely elderly. J Laparoendosc Adv Surg Tech A 2008;18:56–60.
[25] Tucker JJ, Yanagawa F, Grim R, et al. Laparoscopic cholecystectomy is safe but underused in the elderly. Am Surg 2011;77:1014–20.
[26] Dong JH. The idea of precision surgery to promote the innovation and development of biliary surgery. Chin J Digestive Surg 2015;14:11–2.
[27] Ni QH, Zhang YH, He M, et al. Application of 3D-CT Reconstruction in preoperative evaluation and operation planning of hilar cholangiocarcinoma. Chin J Hepatobiliary Surg 2016;22:489–90.
[28] Cao KL, Zhou SZ. The application and reliability of continuous non-invasive arterial blood pressure monitoring in elderly patients during surgery. J North Sichuan Med College 2018;33:858–61.
[29] Meidert AS, Saugel B. Techniques for non-invasive monitoring of arterial blood pressure. Front Med (Lausanne) 2018;4:231.
[30] Zhu ML, Huang YG, Liu XH, et al. Expert consensus on perioperative management of elderly patients in Peking Union Medical College Hospital. Med J Peking Union Medical College Hospital 2018;9:36–41.
[31] Buhrman WC, Lyman WB, Kirks RC, et al. Current state of enhanced recovery after surgery in hepatopancreatobiliary surgery. J Laparoendosc Adv Surg Tech A 2018;28:1471–5.
[32] Xu X, Zheng C, Zhao Y, et al. Enhanced recovery after surgery for pancreaticoduodenectomy: review of current evidence and trends. Int J Surg 2018;50:79–86.

[33] Patel SH, Kim BJ, Tzeng CD, et al. Reduction of cardiopulmonary/renal complications with serum BNP-guided volume status management in posthepatectomy patients. J Gastrointest Surg 2018;22:467–76.
[34] Fan J, Ma J, Xia N, et al. Clinical value of combined detection of CK-MB, MYO, cTnI and plasma NT-proBNP in diagnosis of acute myocardial infarction. Clin Lab 2017;63:427–33.
[35] Zhao K, Tang M, Wang H, et al. Simultaneous detection of three biomarkers related to acute myocardial infarction based on immuno-sensing biochip. Biosens Bioelectron 2019;126:767–72.
[36] Cheng AC, Liao KM, Ho CH, et al. The prognosis in extremely elderly patients receiving orotracheal intubation and mechanical ventilation after planned extubation. Medicine (Baltimore) 2020;99:e21970.