Effect of multimodal prehabilitation on major outcomes of laparoscopic cholecystectomy after emergency percutaneous transhepatic gallbladder drainage in the elderly patients - A real-world based retrospective cohort study

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Research Article

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Abstract

Background & aims:

Multimodal prehabilitation is a new concept of preoperative management. We aimed to study the effectiveness of multimodal prehabilitation in the elderly patients who would receive laparoscopic cholecystectomy (LC) after emergency percutaneous transhepatic gallbladder drainage (PTGBD) .

Methods

This is a retrospective cohort study. Consecutive patients undergoing LC after emergency PTGBD between January 2020 to April 2021 were recruited. Patients over 70years old were treated by multimodal prehabilitation before LC including nutrition support, exercise and psychological interventions as prehabilitation group. Other patients were included as the control group. Perioperative parameters and outcomes were compared between groups.

Results

43 cases were included in this research.24 cases were in the prehabilitation group. Comparing the prehabilitation and control groups, no statistical difference was detected in the laboratory examination before LC except hemoglobin and albumin. There were also no statistical difference in the rates of postoperative complications (8.33%vs.5.26%, P = 0.144) and conversion to open surgery (8.33%vs.5.26%, P = 0.144).

Conclusion

Multimodal prehabilitation could make the rate of major outcomes of LC after emergency PTGBD close to the young patients in the elderly patients.

Introduction

Acute cholecystitis accounts for approximately one-third of surgical emergencies[1], in which, the proportion of elderly patients is increasing. Laparoscopic cholecystectomy (LC) is the most common treatment for acute cholecystitis within 72 hours. However, elderly patients often have one or more comorbidities and possess a higher risk of perioperative complications and mortality if they undergo emergency operation[2]. Percutaneous transhepatic gallbladder drainage (PTGBD) is less invasive than emergency operation and may effectively reduce the tension of gallbladder and toxin absorption. 6-weeks after PTGBD, cholecystectomy could be carried out safely[3, 4].

However, due to the influence of acute inflammation and comorbidities, the general condition may be worsen in the elderly, which may lead to either intolerance of cholecystectomy or higher risk of complications and mortality after the operation[5, 6]. So what we do in the interval between PTGBD and LC may determine the prognosis of the patients.

Preoperative multimodal prehabilitation refers to preoperative multidisciplinary interventions to improve the organs functional reservation, in order to adapt surgical stress and accelerate recovery, which contains nutrition support, exercise and psychological interventions[7]. The concept is new in the field of hepato-billo-pancreatic surgery and few evidence exists. In this study, we conducted multimodal prehabilitation in the interval between PTGBD and LC and did comparison with elective LC to assess the role of prehabilitation in the whole course of treatment of acute cholecystitis especially in the elderly.

Methods

Patients

This research was a retrospective cohort study. Consecutive patients with acute cholecystitis from January 2020 to April 2021 were included in the study group and all the patients fulfilled the inclusion criteria as following: (1).Diagnosis acute cholecystitis confirmed by ultrasound, CT and other ancillary tests,(2) The diagnosis should be in accordance with Tokyo Guidelines 2018 (TG18) grade II who had failed anti-infection treatment and TG18 grade III[8], (3) PTGBD was performed after diagnosis, (4)Prehabilitation was followed up after PTGBD for the patients over 70years, (5) LC was performed 6-8 weeks after PTGBD,(6) Both puncture and surgery were performed by the same team.Figure 1 shows the flowchart of the study.

The study was approved by the institutional research ethics committee of Beijing Hospital in compliance with the Helsinki (Ethic Number: 2021BJYYEC-287-01). The written informed consent was obtained from each subject. Our research had registered at Chinese Clinical Trial Registry and the number was ChiCTR2100053898. The datasets used or analyzed in this study are available from the corresponding authors upon reasonable request.

Interventions in the study group

The study group received a three-stage treatment strategy. We formed a multidisciplinary team containing surgeons, nurses, physicians from the department of nutrition and rehabilitation. In the first stage, PTGBD was done to solve the emergency problem, in the second stage which is the interval between PTGBD and LC lasting 6-weeks, prehabilitation intervention were conducted both in the outpatient clinic and at home by our multidisciplinary team, in the third stage, we did LC. The details are as follows.

Stage I - PTGBD

We did PTGBD under the guidance of ultrasound. Seldinger method was routinely used and 8F pigtail tube was placed through the right intercostal space. Multi-point fixation and lap band protection were done to prevent the tube shedding or displacement.

Stage II - Multimodal prehabilitation

A triple intervention stratage was used after PTGBD[9].

(1) Nutritional support: All patients in the study group received oral nutrition supplement (ONS). According to the ESPEN Guideline: Clinical Nutrition in Surgery, we used "3+3" principles (three meals plus three times of ONS), which was adding ONS between meals and before going to bed. The target of ONS was 400-600kcal/d by providing total protein formula[10].

(2) Exercise intervention: A plan of aerobic training was made by the rehabilitation physician according to patients condition. Patients performed walk daily for a total of 30 minutes as the moderate aerobic exercise and 25 minutes of resistance exercises such as elastic band or dumbbell exercises everyday[11]. Besides muscular exercise, the patients were also instructed to do abdominal breathing exercise at least three times a day, which was inhaling deeply through the nose and holding the breath for 3-4 seconds, and then exhaling through the mouth.

(3) Psychological intervention: All the team members kept in touch with the patients and their relationships. The anxiety and depression level will be evaluated by the HAD score. Patients will be trained to reduce and manage anxiety at home.The intensive follow-up was done by both out clinic interview and on line (telephone or WeChat) in order to solve their problems as soon as possible to relieve the anxiety[12]. Patients were asked to go back to see the surgeons and psychological nurses every two week and psychological guidance was given.

Stage III - LC

6-8 weeks after PTGBD, a preoperative evaluation was done. We reassessed the effect of multimodal prehabilitation, the comorbidities and the indication of LC.

Since former local inflammation and adhesion in the study group, we often opened the gallbladder to find the inner outlet of gallbladder tube to prevent the damage of bile duct. The PTGBD tube was removed at the same time.

Data Collection

(1) Basal data

Gender, age, BMI, comorbidities and age-adjusted Charlson Comorbidity Index(aCCI)were collected from both groups, as well as blood cell count, hemoglobin, platelet, ALT, AST, TBIL, DBIL, TP, ALB, Cr, D-dimer, fibrinogen level. NLR, LMR, PLR were collected.

The number of neutrophils, lymphocytes, monocyte, and platelets can provide information about patient's immune system and inflammatory state. Because neutrophils are considered to interact with other immune cells and platelets, neutrophil-lymphocyte ratio (NLR), lymphocyte-monocyte Ratio (LMR) and platelet-lymphocyte ratio (PLR) can reflect the degree of inflammatory response.

(2) Data before operation

We collected white blood cell count, neutrophil count, hemoglobin level, platelet level, NLR, LMR, PLR, ALT, AST, TBIL, DBIL, TP, ALB, Cr, D-dimer, and Fib levels before LC.

(3) Complications

Complications in this study refer to unexpected events caused by the procedures of LC, including intraoperative biliary tract injury, intraoperative bleeding, abdominal organ injury, abdominal infection and wound infection. We also recorded the complications of PTGBD, containing tube obstruction, shedding and recurrent infection.

Statistics

SPSS 26.0 software was used for statistical analysis. The measurement data were expressed as median (first quartile - third quartile). The test levels $\alpha=0.05$, and $P<0.05$ were considered statistically significant. The Mann-Whitney U test and Wilcoxon test were used for comparison between groups for measurement data that did not obey normal distribution. Count data were expressed as rates, and group comparisons were made using the chi-square tests.

We did two comparisons in this study. Comparison I is to compare the basal data of the two groups. Comparison II is to compare the white blood cell count, neutrophil count, hemoglobin level, platelet level, NLR, LMR, PLR, ALT, AST, TBIL, DBIL, TP, ALB, Cr, D-dimer, Fib level, time of surgery, conversion to laparotomy, abdominal drainage, the occurrence of surgical complications and total cost of hospitalization in the two groups at the time of LC.

Results

A total of 43 cases were included in this research.24 cases which over 70years old were in the prehabilitation group. 19 cases were in the control group.(Fig. 1).

Table 1 shows the general data of the two groups. There were statistically significant differences in age,ASA grade and aCCI between the two groups. Patients in the prehabilitation group were older and had a higher ASA grade and aCCI score.

Table 1 Baseline Characteristics of Patients

	Prehabilitation Group		Control Group		P value
Gender	Male,11 (45.8%)	Female,13 (54.2%)	Male,12 (63.2%)	Female,7 (36.8%)	0.258[b]
Age, median (IQR),y	78(73-84)		64(56-66)		< 0.001[a]
BMI median (IQR)	23.81(22.27-25.71)		26.37(24.13-28.05)		< 0.001[a]
Complication					
Hypertension	15(62.5%)		11(57.9%)		0.759[b]
Diabetes	9(37.5%)		8(42.1%)		0.759[b]
Coronary heart disease	5(20.8%)		2(10.5%)		0.363[b]
Cerebral infarction	6(25.0%)		0(0%)		0.022[b]
Cardiac arrhythmia	3(12.5%)		1(5.3%)		0.398[b]
History of malignancy	4(16.7%)		2(10.5%)		0.453[b]
COPD	1(4.2%)		0(0%)		0.558[b]
Abdominal surgery history	5(20.8%)		4(21.1%)		0.637[b]
ASA grade					0.014[a]
I	3(12.5%)		7(36.8%)		
II	12(50.0%)		10(52.7%)		
III	5(20.8%)		2(10.5%)		
IV	4(16.7%)		0(0%)		
aCCI	6(5-6)		3(3-4)		< 0.001[a]

[a]. Calculated with the Mann-Whitney U test

[b]. Calculated with the χ^2 test

Patients in the prehabilitation group were compared with patients in the control group before LC. Only hemoglobin levels, and albumin levels had statistically significant differences. For the operation, the length of operation, conversion to laparotomy, abdominal drainage, days after operation and the

occurrence of surgical complications were compared between the two groups. There was no significant difference between the two groups in terms of days after operation(P = 0.249), the rate of conversion to laparotomy (P = 0.620) and the incidence of surgical complications(P = 0.694), and the rate of placement of abdominal drains(P = 0.418). All the results was shown in Tables 2.

Table 2
Comparison between the two groups

	Prehabilitation Group	Control Group	P value
WBC ($\times 10^9$/L)	6.62(5.53–7.78)	6.47(5.44–7.72)	0.441[a]
Hb (g/L)	123(112–130)	133(118–142)	0.041[a]
PLT($\times 10^9$/L)	209(177–258)	212(167–245)	0.999[a]
NLR	2.20(1.85–2.52)	1.57(1.39–3.14)	0.399[a]
LMR	4.09(2.76–5.02)	4.09(3.04–5.35)	0.642[a]
PLR	122.08(100.00-170.69)	120(88.89-170.05)	0.448[a]
ALT (IU/L)	16(11–27)	20(16–32)	0.106[a]
TBIL (μmol/L)	10.5(7.4–18.3)	13.4(8.7–19.3)	0.287[a]
DBIL (μmol/L)	3.7(2.7–6.4)	4.1(2.8–7.6)	0.599[a]
TP (g/L)	66(63–68)	66(64–67)	0.797[a]
ALB (g/L)	37(35–39)	40(38–40)	0.006[a]
Cr (μmol/L)	63(59–79)	64(59–70)	0.624[a]
AST (IU/L)	19(16–24)	21(17–25)	0.405[a]
D-dimer(ng/ml)	301(148–412)	158(96–204)	0.115[a]
Fib(g/L)	3.10(2.67–4.20)	3.15(2.92–3.32)	0.941[a]
Length of operation(min)	80(70–110)	100(80–120)	0.113[a]
Total cost(USD)	3365.30(2829.41-4799.73)	3301.01(2526.59-4536.19)	0.525[a]
Days after operation (d)	5(3–9)	4(2–5)	0.249[a]
Complication	1(4.17%)	1(5.26%)	0.694[b]
Conversion to laparotomy	2(8.33%)	2(10.52%)	0.620[b]
Drainage	12(50.00%)	11(57.89%)	0.418[b]

[a]. Calculated with the Mann-Whitney U test

[b]. Calculated with the χ^2 test

Discussion

Laparoscopic cholecystectomy (LC) is still the main treatment for acute cholecystitis. However, the incidence of surgical complications is relatively high in patients with elderly, more comorbidities, and severe infection [13]. PTGBD is used as a transitional therapy to reduce the patient's gallbladder tension and drainage bile through the puncture, thus achieving the goal that converting emergency operation to elective. Preoperative prehabilitation is now widely used in clinical as a method to improve the prognosis of surgical patients [14].

Although there were still differences in some lab indexes, the patients in the prehabilitation group were older and had higher ASA grades than the control group. But there was no significant difference in the rate of complications occur and conversion to laparotomy between the two groups. Dragos et al. showed that the rate of conversion to laparotomy in LC patients over 50 years of age was 7.2%-17.6% and the rate of surgical complications was 5.8%-9.1%, both of which were significantly higher than those in patients under 50 years[15]. Therefore, patients can still achieve similar clinical outcomes after preoperative prehabilitation, although the preoperative indexes were not as good as the elective.

Preoperative prehabilitation consists of three main parts: nutritional support, individualized exercise interventions, and preoperative psychological interventions [16]. A higher incidence of malnutrition in elderly patients over 65 years can increase the incidence of perioperative complications and increases postoperative recovery time[17]. In a study of 61 patients undergoing surgery for IBD, Fiorindi et al. found that after preoperative oral nutritional support, despite weight loss the body composition was not changed. It suggests that preoperative nutritional support has a protective effect on the consumption of non-adipose tissue, particularly muscle tissue during the perioperative period[18]. In addition, oral nutritional support has been shown to improve the preoperative nutritional status of patients as well as to regulate intestinal flora. Animal studies by Keskey et al. demonstrated that the mice were treated with low-fat, high-fiber preoperative nutritional support. After that, they were operated partial hepatectomy and prophylactic used antibiotics. The number of butyrate-producing bacteria in the intestinal was increased because butyrate could reduce the inflammatory response of the intestinal[19].

Marjanski et al. showed that a 6-minute walk test was effective in assessing patients' preoperative cardiopulmonary reserve and was strongly associated with patient prognosis[20]. Therefore preoperative exercise training helps patients early recovery activities after surgery and achieve rapid recovery. A meta-analysis by Christina et al. showed that the postoperative 6-minute walk test distance was significantly longer in the prehabilitation group than in the control group[21]. Exercise interventions for patients still need to be individualized[12]. For patients with normal exercise capacity, their exercise can be divided into aerobic and resistance exercise, which is 50% for each[22]. In our research, the median age of patients in the PTGBD group was more than 70 years old, which the oldest being 92 years old. For such elderly patients, appropriate exercise programs can be planned according to the patient's general condition and

tolerance. Transitional exercise is not advisable. In addition, for patients undergoing abdominal surgery, their respiratory muscle function should be trained preoperatively to increase respiratory function reserve and improve patients' lung function to reduce the occurrence of respiratory complications such as postoperative pneumonia.

The unhealthy status can lead to an increased psychological burden on the patient, which can be detrimental to the patient's post-operative recovery. Wang et al. found that the high levels of IGF-1 and IGFBP-3 in the brains of preoperative patients were highly correlated with anxiety and depression [23]. Studies show that 30% of patients with preoperative fear and anxiety require psychological intervention[24]. Louise suggests attention training, self-regulation, guidance on correct values, and setting relevant milestones to eliminate fear and worry[25]. However, psychological interventions are difficult to implement in outpatient clinics and wards, and patients' compliance and cooperation are difficult to ensure. This has led to a new concept in recent years: family-based preoperative psychotherapeutic interventions. In the Roshan et al. study, patients were instructed in values-based goal setting, self-behavior management, relaxation, and positive breathing exercises, cognitive reconstruction, and post-operative planning before surgery by creating a treatment manual, which taking place at home for approximately one hour at a time, once or twice a week by the patients themself[26]. This method is simple and easy to follow and patients are more likely to cooperate.

In this study, the prehabilitation group were older and had more comorbidities. Patients who received prehabilitation interventions before surgery had improved and enhanced their preoperative physiological reserve and psychological status so that they could optimally endure the upcoming surgery and in this study we could see a significant improvement in their functional status before surgery. There was no significant difference in preoperative baseline laboratory tests, and there was no statistically significant difference in the incidence of surgical complications and intermediate open surgery rates between the two groups.

The aging of surgical patients, concomitant multiple underlying diseases, and acute infections are characteristics that often accompany risk factors for postoperative complications such as malnutrition and abnormal immune function, resulting in a longer preoperative preparation time and a slower postoperative recovery process. However, due to the application of PTGBD-prehabilitation interventions, high-risk elderly patients with sever acute cholecystitis and comorbidities have been given the opportunity to surgery, which reflecting the value of prehabilitation.

This study still has some limitations. It is a retrospective study with a small sample size, there is still a need to increase the sample size and further refine the prehabilitation protocol for LC patients. A prospective randomized controlled trial should also be conducted to further confirm the role of preoperative prehabilitation in the perioperative period, especially in elderly patients whose benefits are still to be proven.

Abbreviations

WBC	White Blood Cells
Hb	Hemoglobin
PLT	Platelet
NLR	Neutrophil To Lymphocyte Ratio
LMR	Lymphocyte To Monocyte Ratio
PLR	Platelet To Lymphocyte Ratio
ALT	Alanine Aminotransferase
TBIL	Total Bilirubin
DBIL	Direct Bilirubin
TP	Total Protein
ALB	Albumin
Cr	Creatinine
AST	Aspartate Aminotransferase
Fib	Fibrinogen

Declarations

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Competing interest:

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. The authors declare no conflict of interest.

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All authors have read and approved the final manuscript.

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Figures

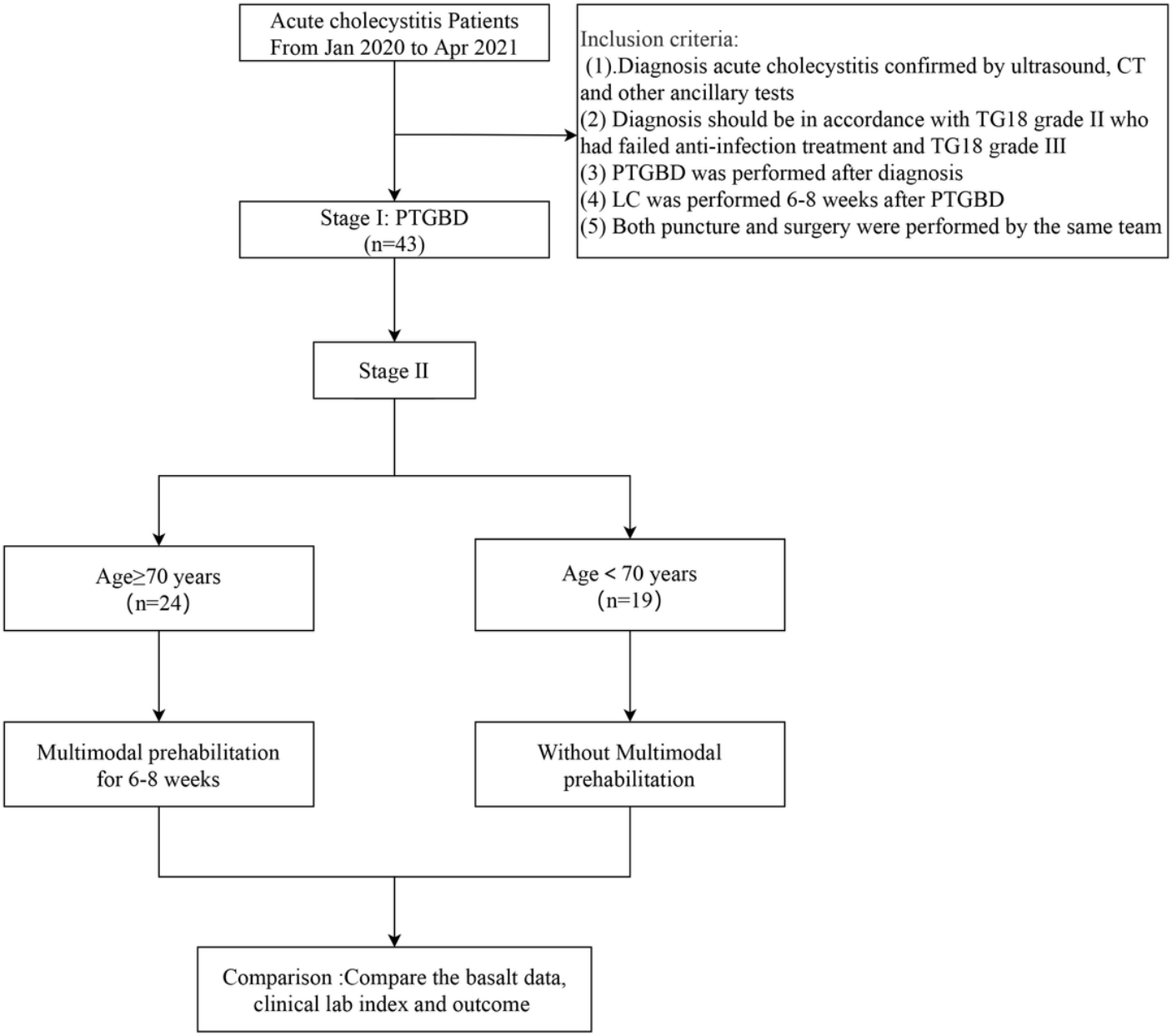

Figure 1

flow chart of this research