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Original Article

Effect of timing of laparoscopic cholecystectomy on postoperative efficacy and rehabilitation of elderly patients with acute cholecystitis

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Abstract: Objective: To discuss the effect of the timing of laparoscopic cholecystectomy (LC) on postoperative efficacy and rehabilitation in elderly patients with acute cholecystitis (AC). Methods: Ninety-four elderly patients with AC were retrospectively selected and assigned into a research group (n=47) and a control group (n=47). The research group was administered LC within 48 hours after the onset. The control group was administered LC 48 hours after the onset. The two groups were compared for perioperative parameters, bilirubin and immune function, concentration of inflammatory factors, stress response, energy metabolism, and complications. Results: The research group had a shorter operation time, hospital stay, and less intraoperative blood loss than the control group (all $P<0.05$). No significant intergroup difference was found in the anal exhaust time ($P>0.05$). The levels of postoperative direct bilirubin, total bilirubin, γ-glutamyl transpeptidase, alkaline phosphatase, serum CRP, TNF-α, and IL-6 were lower than those measured preoperatively in both groups (all $P<0.001$), and were lower in the research group than in the control group (all $P<0.05$). The postoperative pulse, diastolic pressure, and systolic pressure in the two groups were higher than those measured preoperatively (all $P<0.001$). The levels in the research group were lower than those in the control group (all $P<0.001$).The levels of adenosine triphosphate and adenosine diphosphate also decreased in both groups, but they were still higher in the research group than those in the control group (all $P<0.001$). The incidence of complications in the research group (4.26%) was lower than that in the control group (17.02%; $P<0.05$). Conclusion: Early LC in elderly patients with AC is beneficial to postoperative functional rehabilitation, showing less impact on energy metabolism, lower stress response caused by surgery, lower bilirubin content, less inflammatory reaction, better liver function, and lower incidence of complications in patients.

Keywords: Elderly acute cholecystitis, laparoscopic cholecystectomy, timing of operation, functional rehabilitation

Introduction

Acute cholecystitis (AC) in elderly patients is a cholecystitis lesion with a high incidence caused by cystic duct obstruction, bacterial invasion, and chemical stimulation. Most of the patients are accompanied with right upper abdominal pain, which can spread to the right shoulder and back. Some of the patients are complicated with vomiting, nausea, and fever. If the disease is not effectively intervened, it will lead to many complications and increase disease mortality risk [1]. For elderly patients with AC, conservative intervention (including maintaining acid-base balance, correcting water-electrolyte disturbance, and spasmolysis) is usually the first step in clinical practice. Some patients are still difficult to achieve favorable outcomes, and suffer from biliary obstruction, biliary colic, and pancreatitis [2]. In recent years, with the popularization of minimally invasive concept and the continuous improvement of medical technology, the indications of laparoscopic cholecystectomy (LC) have been expanding, and its application value in AC has gradually attracted extensive attention [3]. The body's stress ability decreases after the onset of AC. Most elderly patients are complicated with different types of underlying diseases. Some scholars believe that the early implementation of LC to these patients may lead to a high risk of death. There is still some controversy on the best timing of intervention [4]. Based on the above background, this study intended to explore the effect of LC timing on postoperative efficacy and rehabilitation of elderly AC patients.

Materials and methods

The baseline data

Ninety-four elderly patients with AC admitted to Rudong Hospital Affiliated to Nantong University from January 2020 to July 2021 were selected retrospectively and assigned into a research group (n=47) and a control group (n=47) according to operative methods. Inclusion criteria: (1) Patients who met the diagnostic criteria of AC [5], and their Murphy's sign was positive with right upper abdomen tenderness; (2) Patients with an age of ≥60 years old; (3) Patients accompanied with varying degrees of vomiting, nausea, and fever; (4) Patients with LC indications [5]. Exclusion criteria: (1) Patients with organic diseases of kidney and liver; (2) Patients with diseases of blood system and endocrine system; (3) Patients with other infectious diseases. (4) Patients with pancreatitis and bile duct stones; (5) Patients with previous history of laparotomy; (6) Patients treated with immune stimulants or hormone drugs within 3 months before being included in the study; (7) Patients with malignant tumors. This study was approved by the ethics committee of Rudong Hospital Affiliated to Nantong University. The patients or their families signed the informed consent.

Methods

The research group received LC within 48 hours (who conducted relevant examinations after admission) after the onset. The control group was treated by LC 48 hours after the onset (the patients received conservative treatment first, and then underwent the selective operation after the inflammation and clinical symptoms were relieved). The specific steps of LC were as follows [6]: With the supine position taken, the three-port technique was used. After general anesthesia, the skin 1 cm above the umbilicus was cut open, and a pneumoperitoneum needle was inserted into it. When the sense of loss occurred twice, it indicated that the test water had entered the abdominal cavity. The pneumoperitoneum machine was connected, and the pressure value was set to 13 mmHg. The trocar (10 mm) was placed in the umbilicus, and the endoscope was used to determine if there was puncture side injury. After confirming that there was no exudation and active bleeding in the abdominal cavity, the skin was cut 1.2 cm below the xiphoid by the aiding of endoscope. The trocar (12 mm) was inserted into the abdominal cavity through the right side of the hepatic round ligament. The trocar (5 mm) was inserted 2 cm below the costal edge of the right axillary front by cutting open the skin 0.5 cm. The patients were assisted to take the head-high-foot-low position, and the left oblique position was taken to facilitate the operation. The adhesion around the gallbladder was separated, the gallbladder triangle was exposed, and the serosa was separated to clarify the relationship between the three tubes. The cystic duct and cystic artery were separated. A plastic clip was applied at the proximal end and at the distal end of the cystic duct to avoid bile outflow from the gallbladder. The cystic duct was cut between the two clips. The stump was 0.3 cm away from the plastic clip and 0.6 cm away from the common bile duct. The anterior and posterior branches of the cystic artery were clipped with plastic clips and cut off. The cystic duct was pulled upwards to expose the loose connective tissue between the gallbladder and the liver bed. This was stripped to avoid injury to the gallbladder and bleeding from the liver wound. It was then separated from bottom to up to the bottom of the gallbladder to complete the cholecystectomy operation. The gallbladder forceps were used to clamp the gallbladder neck and the puncture part under the xiphoid (including Trocar) and pull it out of the body. The periphery was covered with gauze to protect the incision, the plastic clip was removed, and the gallbladder was taken out. Electrocoagulation hemostasis was performed on the gallbladder bed to determine if there was active bleeding under the right diaphragm, the liver, or each trocar hole. The peritoneal effusion was cleared, and the fluid glue was sprayed on the wound of the gallbladder bed. Based on specific conditions, it was determined if the drainage tube needed to be placed under the liver.

Table 1. Comparison of the baseline data of the two groups ($\bar{x}$ ± sd, n)

Groups	Research Group (n=47)	Control Group (n=47)	χ^2/t	P
Gender (male/female)	28/19	30/17	0.180	0.671
Age (Y)	76.3±10.8	74.9±11.3	0.614	0.541
Underlying Diseases				
Diabetes	6 (12.77)	9 (19.15)	0.714	0.398
Hypertension	16 (34.04)	11 (23.40)	1.299	0.254
Others	4 (8.51)	2 (4.26)	0.178	0.673
BMI (kg/m^2)	19.03±3.18	18.79±3.41	0.353	0.725
Disease Classification			1.792	0.408
Simple Type (n)	22 (46.81)	24 (51.06)		
Gangrene Type (n)	7 (14.89)	3 (6.38)		
Purulent Type (n)	18 (38.3)	20 (42.55)		

Note: BMI: body mass index.

Measured outcomes

(1) The baseline data including gender, age, underlying diseases, body mass index, and disease classification of the two groups were counted. (2) The perioperative conditions including operation time, intraoperative blood loss, anal exhaust time, and hospital stay of the patients in the two groups were counted. (3) The levels of bilirubin, direct bilirubin (DBIL), total bilirubin (TBIL), the liver function indexes, γ-glutamyl transpeptadase (GGT), and alkaline phosphatase (ALP) before and after surgery were measured. Blood samples were taken, and the above index levels were measured by Hitachi 7600 automatic biochemical analyzer. (4) The concentration of serum inflammatory factors, C reactive protein (CRP), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6), were measured pre- and post-operatively. After the blood samples were taken for centrifugation (3000 r/min, 10 min), the supernatant was taken for detection of the above index by enzyme-linked immunosorbent assay. The kits (Batch Numbers ml057570, ml077385, and ml058097, respectively) were purchased from Shanghai Mlbio, China. (5) The levels of stress response indexes (pulse and blood pressure) before and postoperative were measured. (6) The serum energy metabolism indexes adenosine triphosphate (ATP) and adenosine diphosphate (ADP) were determined pre- and post-operatively. Blood samples were taken and determined by automatic biochemical analyzer (Hitachi 7600). After the blood samples were taken, supernatant was centrifuged for determination by ELISA. The kits (Batch Numbers 200112 and 200407) of ATP and ADP were purchased from Shanghai Jianglai Biotechnology, China. (7) The incidence of complications (organ injury, intestinal obstruction, urinary tract infection, and bile leakage) in the two groups was counted. The incidence of complications = the number of cases with complications/total number of cases *100%.

Statistical methods

SPSS 22.0 software was used for data analyses. Graphpad Prism 6.0 was used for plotting statistical figures. The measured data were expressed as $\bar{x}$ ± sd and tested by t-test. The enumeration data were expressed as n (%) and tested by χ^2-test. $P<0.05$ indicated that the difference was statistically significant.

Results

Comparison of the baseline data

No significant intergroup difference was observed in gender, age, underlying diseases, body mass index, and disease classification (all P>0.05). See **Table 1**.

Comparison of perioperative conditions

The research group showed shorter operation time and hospital stay, and a lower amount of intraoperative blood loss than the control group (all P<0.05). No significant intergroup difference was found in anal exhaust time (P>0.05). See **Table 2**.

Comparison of bilirubin and liver function

No significant intergroup difference was found in the preoperative levels of DBIL, TBIL, GGT, and ALP (all P>0.05). The postoperative levels of DBIL, TBIL, GGT, and ALP in the two groups were lower than those measured preoperatively, and lower in the research group than in the control group (all P<0.05). See **Table 3**.

Comparison of inflammatory factors

No significant intergroup difference was observed in the levels of serum CRP, TNF-α,

Table 2. Comparison of perioperative conditions between the two groups ($\bar{x}$ ± sd)

Groups	Operation Time (min)	Anal Exhaust Time (h)	Hospital Stay (d)	Intraoperative Blood Loss (mL)
Research group (n=47)	56.91±20.11	31.26±8.91	4.46±1.25	79.36±22.08
Control Group (n=47)	66.64±19.51	33.35±9.38	6.73±1.59	130.19±30.24
t	2.381	1.108	7.695	9.307
P	0.019	0.271	0.000	0.000

Table 3. Comparison of bilirubin and liver function indexes between the two groups ($\bar{x}$ ± sd)

Groups	DBIL (umol/L)	TBIL (umol/L)	GGT (U/L)	ALP (U/L)
Preoperative				
Research group (n=47)	81.35±13.32	111.37±32.95	89.95±13.21	146.97±26.53
Control group (n=47)	79.96±11.78	108.79±35.04	91.69±11.64	150.22±23.12
t	0.536	0.368	0.678	0.633
P	0.593	0.714	0.500	0.528
Postoperative				
Research group (n=47)	13.35±3.51***	32.14±5.61***	41.55±7.02***	39.96±8.23***
Control Group (n=47)	20.04±5.11***	41.29±6.88***	50.24±6.71***	49.38±9.66***
t	7.398	7.066	6.135	5.089
P	<0.001	<0.001	<0.001	<0.001

Note: Compared with this group preoperative, ***P<0.001. DBIL: direct bilirubin; TBIL: total bilirubin; GGT: γ-glutamyl transpeptidase; ALP: alkaline phosphatase.

Table 4. Comparison of inflammatory factors between the two groups ($\bar{x}$ ± sd)

Time	Groups	n	TNF-α (ng/L)	IL-6 (ng/L)	CRP (mg/L)
Preoperative	Research group	47	18.56±5.71	18.12±4.54	30.67±5.67
	Control group	47	20.50±6.23	20.20±6.61	32.04±6.11
	t		1.574	1.778	1.127
	P		0.119	0.079	0.263
Postoperative	Research group	47	9.58±2.14***	6.93±1.89***	12.67±3.85***
	Control group	47	12.71±3.33***	9.06±2.11***	16.56±4.19***
	t		5.421	5.155	4.687
	P		<0.001	<0.001	<0.001

Note: Compared with this group preoperative, ***P<0.001. TNF-α: tumor necrosis factor-α; IL-6: interleukin-6; CRP: C reactive protein.

and IL-6 preoperatively (all P>0.05). The postoperative levels of serum CRP, TNF-α, and IL-6 were lower than those measured preoperatively in both groups, and were lower in the research group than in the control group (all P<0.001). See **Table 4**.

Comparison of stress response

No significant intergroup difference was found in pulse, diastolic pressure, and systolic pressure preoperatively (all P>0.05). The postoperative levels were higher than those measured preoperatively in both groups, but they were lower in the research group than those in the control group (all P<0.001). See **Table 5**.

Comparison of energy metabolism indexes

There was no significant intergroup difference in the levels of ATP and ADP preoperatively (all P>0.05). The postoperative levels of ATP and ADP in the two groups were lower than those measured preoperative (all P<0.001). The lev-

Table 5. Comparison of stress response indexes between the two groups ($\bar{x}$ ± sd)

Time	Groups	n	Diastolic pressure (mmHg)	Systolic pressure (mmHg)	Pulse (times/min)
Preoperative	Research group	47	89.13±6.54	127.97±9.06	87.69±7.78
	Control group	47	88.21±5.68	130.24±8.65	88.71±8.11
	t		0.728	1.242	0.622
	P		0.468	0.217	0.535
Postoperative	Research group	47	95.09±6.38***	135.41±7.79***	95.96±7.33***
	Control group	47	101.15±8.26***	141.04±8.19***	106.34±8.81***
	t		3.981	3.415	6.209
	P		0.000	0.001	0.000

Note: Compared with this group preoperative, ***P<0.001.

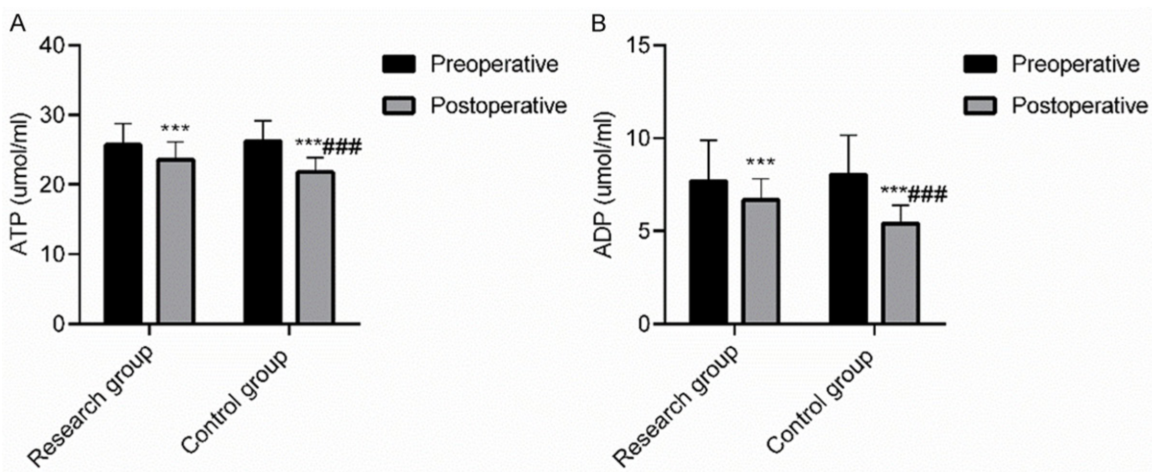

Figure 1. Comparison of energy metabolism indexes between the two groups. The levels of ATP (A) and ADP (B) were higher in the research group than those in the control group. Compared with this group preoperative, ***P<0.001; compared with the research group, $^{\#\#\#}$P<0.001. ATP: serum adenosine triphosphate; ADP: adenosine diphosphate.

Table 6. Comparison of the incidence of complications between the two groups (n, %)

Groups	n	Organ injury	Intestinal obstruction	Urinary tract infection	Bile leakage	Total incidence
Research group	47	0 (0.00)	1 (2.13)	1 (2.13)	0 (0.00)	2 (4.26)
Control group	47	1 (2.13)	3 (6.38)	2 (4.26)	2 (4.26)	8 (17.02)
χ^2						4.029
P						0.045

els of ATP and ADP in the research group were higher than those in the control group (all P<0.001). See **Figure 1**.

Comparison of complications

The incidence of complications in the research group (4.26%) was lower than that in the control group (17.02%; P<0.05). See **Table 6**.

Discussion

AC is a multiple acute abdomen conditions. Elderly patients are often complicated with diabetes and hypertension. With the poor liver filtration, they are prone to cholecystolithiasis providing a good environment for bacterial proliferation, which causes infection and suppuration [7, 8]. As an important minimally invasive treatment measure for clinical treatment of AC, LC is beneficial to the early rehabilitation of postoperative body function with less trauma and high safety. There is still some controversy about its best timing for treatment [9, 10].

In this study, LC was used to treat elderly patients with AC in our hospital at different time points. The results showed that the perioperative conditions of the research group were better than those of the control group. The levels of TNF-α, IL-6, CRP, pulse, diastolic blood pressure, and systolic blood pressure were more improved in the research group than those of the control group. This is consistent with the research results of Borzellino [11] and Ismael Mora-Guzman [12]. It is indicated that early LC is better than selective LC treatment in reducing surgical trauma and the degree of inflammatory reaction and stress response caused by invasive operation. It is also conducive to the early rehabilitation of body function. The reason is that the early course of the disease is relatively short, the degree of cystic paries edema is relatively light, the tissue is relatively loose, and it is easy to be separated with the assistance of endoscopy. The anatomical relationship between the hepatocholedchus and cystic duct can be identified accurately. The relevant treatment operations also can be conducted accurately. This can reduce the risk of damaging the gallbladder and other organs in the abdominal cavity. After the acute attack of the disease, the gallbladder infection continues to progress. The degree of adhesion between the tissues intensifies, and tends to be tight. This is not conducive to the operation, and it is easy to damage the surrounding organs [13]. Selective LC treatment may cause delayed cholecystectomy and focus cleaning, resulting in severe postoperative inflammatory response to aggravate body injury and affect postoperative rehabilitation [14]. This study also showed that the postoperative levels of DBIL, TBIL, GGT, and ALP in the research group were higher than those in the control group ($P<0.05$), which is consistent with the results of Wiggins et al. [15]. It is suggested that compared with selective LC, early LC is conducive to regulating the serum bilirubin and improving the liver function. This is mainly because early surgical treatment can timely and effectively remove the lesions and avoid the aggravation of inflammatory reaction and stress reaction in the body [16, 17]. This study showed that the postoperative levels of ATP and ADP in the research group were higher than those in the control group, indicating that early LC has more advantages than selective LC in reducing the metabolic impact of surgery on elderly AC patients. It may be because the early LC operation is relatively simple and the anatomical level is clear, which is convenient for surgical separation. With the extension of the course of disease, tissue adhesion intensifies, and the anatomical level is not clear, resulting in increased intraoperative blood loss and possible damage to peripheral organs and tissues. Early LC is conducive to reducing the degree of inflammatory reaction and stress response caused by invasive operation, reducing the impact of surgical treatment on the body's energy metabolism [18, 19]. According to the results of this study, the incidence of complications in the research group was lower than that in the control group. Sladecek et al. also pointed out that early implementation of LC treatment could reduce the incidence of complications in AC patients. This indicated that early implementation of LC treatment can also effectively reduce the risk of postoperative complications in elderly patients with AC [20]. It may be that the lesions in the early stage of the disease are usually not easy to involve the Calot triangle. In the later stage, with the aggravation of inflammation, it can lead to the formation of adhesive scar, resulting in abnormal anatomical structure in this range, increasing the risk of complications [21].

There are still some limitations in this study. This study is a single center small sample study and lacks follow-up observation on patients. The impact of different operation timing on the prognosis of elderly AC patients and whether the results of this study have broad effectiveness still need to be explored and confirmed by prolonging the follow-up observation time.

In conclusion, early LC treatment of elderly patients with AC is beneficial to postoperative functional rehabilitation and has little impact on energy metabolism. Compared to LC treatment after 48 hours, earlier LC treatment is worthy of promotion because of milder stress reactions, lower bilirubin content, reduced level of inflammatory reaction, improved liver function and reduced incidence of complications.

Disclosure of conflict of interest

None.

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