

Operative stress response and energy metabolism after laparoscopic cholecystectomy compared to open surgery

Kai Luo, Jie-Shou Li, Ling-Tang Li, Kei-Hui Wang, Jing-Mei Shun

Kai Luo, Jie-Shou Li, Ling-Tang Li, Kei-Hui Wang, Jing-Mei Shun, Research Institute of General Surgery, Nanjing General Hospital, Nanjing Command of People's Liberation Army, and Clinical School of Medical College, Nanjing University, Nanjing Jiangsu Province 210002, China

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Correspondence to: Dr. Kai Luo, Research Institute of General Surgery, Nanjing General Hospital, Nanjing Command of People's Liberation Army, and Clinical School of Medical College, Nanjing University, Nanjing 210002, Jiangsu Province, China. lokai@jlonline.com

Telephone: +86-25-4491878

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Abstract

AIM: To determine the least invasive surgical procedure by comparing the levels of operative stress hormones, response-reactive protein (CRP) and rest energy expenditure (REE) after laparoscopic (LC) and open cholecystectomy (OC).

METHODS: Twenty-six consecutive patients with noncomplicated gallstones were randomized for LC (14) and OC (12). Plasma concentrations of somatotropin, insulin, cortisol and CRP were measured. The levels of REE were determined.

RESULTS: In the third postoperative day, the insulin levels were lower compared to that before operation ($P < 0.05$). In the first postoperative day, the levels of somatotropin and cortisol were higher in OC than those in LC. After operation the parameters of somatotropin, CRP and cortisol increased, compared to those in the preoperative period in the all patients ($P < 0.05$). In the all-postoperative days, the CRP level was higher in OC than that in LC (7.46 ± 0.02 ; 7.38 ± 0.01 , $P < 0.05$). After operation the REE level all increased in OC and LC ($P < 0.05$). In the all-postoperative days, the REE level was higher in OC than that in LC (1438.5 ± 418.5 ; 1222.3 ± 180.8 , $P < 0.05$).

CONCLUSION: LC results in less prominent stress response and smaller metabolic interference compared to open surgery. These advantages are beneficial to the restoration of stress hormones, the nitrogen balance, and the energy metabolism. However, LC can also induce acidemia and pulmonary hypoperfusion because of the pneumoperitoneum it uses during surgery.

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INTRODUCTION

The superiority of laparoscopic cholecystectomy (LC) has justified its universal usage in recent years. It induces less

surgical response compared to open cholecystectomy (OC). A great many literatures had proved such an advantage^[1-4]. However, there were few studies concerning the difference between LC and OC in operative stress response and energy metabolism. In this prospective, randomized study, we compared the effects of LC and OC on body oxygen supply, metabolic hormones and response-reactive protein (CRP) levels, body energy metabolism, and acid-base balance.

MATERIALS AND METHODS

Clinical data

Twenty-six patients with uncomplicated gallstones were recruited for the study from April 2001 to Oct. 2001. They were randomized to undergo LC ($n=14$) or OC ($n=12$). The two groups of patients had comparable demographic data (Table 1). All enrolled patients were asymptomatic for at least 6 weeks prior to admission without any history of abdominal surgery. Ultrasonography was routinely performed to exclude the common bile duct stone. The patients with jaundice, severe infection, or metabolic abnormalities were also excluded in this study. Anesthesia was induced and maintained using a standard intravenous protocol in both groups. LC was undertaken by a standard 4-trochar approach with electrocautery dissection; pneumoperitoneum was established with carbon dioxide (CO₂) insufflation, and OC was performed via a sub-costal incision.

Table 1 Comparison of general conditions between the two groups

Group	Number	M/F	Median age (yrs)	Height (cm)	BW (Kg)
OC	12	3/9	45.5±12.6	161.3±7.1	61.0±3.6
LC	14	6/8	46.6±15.8	163.9±6.1	65.8±9.4

Blood samples and evaluation method

Fast venous blood was taken at 6 AM on the day prior to surgery, and days 1 and 3 postoperatively. Samples should be analyzed within 2 hours after stored *in vitro*. All hormones were quantitatively assayed. In CRP assay, rate immunonephelometry with specific protein analyzer (BN 100 Analyzer) was adopted. Growth hormones (GH) levels were determined by double-antibody RIA with reagents from Jiuding Bio-medical Co. Ltd, Tianjing. Serum cortisol and insulin analysis were both carried out by competitive RIA, using reagents from 3V Diagnostic Technique Co. Ltd. and Chinese Institute of Atomic Energy, respectively.

Energy metabolism was assessed by indirect calorimeter on the day prior to operation, and days 1 and 3 postoperatively. During analysis, patients should be reposed, with ambient temperature 18-26 °C and humidity 50-60 %. Oxygen consumption (VO₂) and CO₂ production (VCO₂) per unit time were determined at first. Then, based on the indirect calorimetry theory, REE and RQ were figured out according to the value of VO₂ and VCO₂. All energy consumption measurements were carried out using Medical Graphics Critical Care Monitor Desktop Analysis System (Medical Graphics Co.,

Minneapolis, MN). Artery and acid-base balance were assayed by automatic gas analyzer.

Statistical analysis

Data were given as means and standard error of the mean. The intergroup comparison was made using the Student's *t* test. All the statistical procedures were accomplished with SPSS 8.0. A two-tailed $P < 0.05$ was taken as significant.

RESULTS

Median surgical duration was not different between the LC (50.9±8.9 min) and OC (58.5±6.3 min) group ($P > 0.05$), while the length of hospital stay and the time to first passage of flatus were significantly shorter in LC than those in OC group (Table 2).

Table 2 Postoperative intestinal transit recovery

	OC (n=12)	LC (n=14)
Time to first passage of flatus (days)	2.8±0.4	1.5±0.3 ^a
Postoperative length of stay (days)	6.7±0.2	3.2±0.3 ^a

^a $P < 0.05$ vs OC.

Insulin levels rose significantly on the 3rd postoperative day above baseline measurements in OC group, with no intergroup difference throughout the postoperative period. GH levels elevated in both groups at all phases postoperatively. However, there was a more prominent response in patients undergoing OC. A significant intergroup difference was detected on day 1 following operation with higher values for OC than that for LC. Cortisol levels increased from baseline on both of the postoperative days in the two groups, but more remarkably in OC group. Intergroup comparison indicated that concentrations were significantly higher in patients undergoing OC on day 1, postoperatively. But on the 3rd postoperative day, cortisol concentrations were comparable in the two groups (Table 3).

Table 3 GH, Insulin, and cortisol levels before and after surgery

	Prior to surgery	1st postoperative day	3rd postoperative day
Insulin			
LC (n=14)	14.4±2.1	16.1±2.8	14.6±2.5
OC (n=12)	17.9±2.1	17.2±3.4	12.3±0.9 ^b
GH			
LC	1.0±0.2	2.7±1.0 ^{ab}	1.5±0.5 ^b
OC	1.8±0.4	5.4±2.5 ^b	2.2±0.9
Cortisol			
LC	0.46±0.01	0.56±0.11 ^{ab}	0.74±0.05 ^b
OC	0.71±0.15	1.12±0.25 ^b	0.89±0.02 ^b

^a $P < 0.05$, vs OC ^b $P < 0.05$, vs the preoperative period.

In OC groups, REE levels raised 165.3Kcal from baseline on day 1 postoperatively. The difference was significant. But on the 3rd postoperative day, it was 57.3Kcal higher than baseline only (not significant). A similar pattern was seen in the patients undergoing LC, and there was a marked increase (60.1Kcal) on day 1 but not on day 3. On both of the postoperative days, REE levels were significantly higher in OC than those in LC group. RQ fell significantly from baseline on the 1st postoperative day in both groups. There was a significant elevation of CRP concentrations from baseline

levels in both groups. However, in patients undergoing OC, the increase was more remarkable. CRP levels were significantly higher in OC than those in LC group on both of the postoperative days (Table 4).

Table 4 REE, RQ, and CRP levels before and after surgery

	Prior to surgery	1st postoperative day	3rd postoperative day
REE			
LC (n=14)	1162.2±159.6	1222.3±180.8 ^{ab}	1152.8±150.2 ^a
OC (n=12)	1273.2±304.8	1438.5±418.5 ^b	1330.5±353.8
RQ			
LC	0.87±0.10	0.78±0.06 ^b	0.85±0.09
OC	0.88±0.12	0.78±0.04 ^b	0.84±0.08
CRP			
LC	8.00±0.01	15.10±2.47 ^{ab}	34.44±7.88 ^{ab}
OC	12.37±3.55	64.50±15.20 ^b	94.25±13.43 ^b

^a $P < 0.05$, vs OC ^b $P < 0.05$, vs the preoperative period.

Artery oxygen pressure did not change remarkably after surgery in OC group, while it declined significantly on the 1st postoperative day in the LC group and returned to preoperative levels on the 3rd day. Oxygen saturation (SO₂) in blood fell significantly on the 1st postoperative day in both groups. On the 3rd day, it was much higher in LC than that in OC group. There was no significant change of PCO₂ in both groups after surgery. (Table 5) On the 3rd postoperative day, HCO₃⁻ level and BE rose significantly in LC group, and BE was significantly higher in LC than that in OC group. PH was significantly lower in LC than that in OC group on the 1st postoperative day (Table 6).

Table 5 Artery PO₂, PCO₂ and SO₂ before and after surgery

	Prior to surgery	1st postoperative day	3rd postoperative day
PO₂			
LC (n=14)	87.7±4.0	75.9±3.2 ^b	80.94±4.3
OC (n=12)	80.2±2.2	86.5±9.2	79.81±0.6
PCO₂			
LC	36.79±1.19	37.09±1.64	34.48±1.75
OC	35.01±1.76	31.83±2.63	37.96±1.88
SO₂			
LC	96.4±0.40	94.6±0.86 ^b	95.4±0.40 ^a
OC	95.4±0.40	92.73±1.70 ^b	94.0±0.67

^a $P < 0.05$, vs OC ^b $P < 0.05$, vs the preoperative period.

Table 6 REE, RQ, and CRP levels before and after surgery

	Prior to surgery	1st postoperative day	3rd postoperative day
REE			
LC (n=14)	22.5±0.61	21.7±0.61	22.15±0.83
OC (n=12)	21.02±0.58	20.32±2.1	24.8±0.72 ^b
RQ			
LC	-1.77±0.48	-2.85±0.46	-1.77±0.78 ^a
OC	-1.66±0.54	-2.17±1.38	1.23±0.65 ^b
CRP			
LC	7.40±0.006	7.387±0.008 ^a	7.43±0.008 ^b
OC	7.42±0.013	7.46±0.022	7.44±0.018

^a $P < 0.05$, vs OC ^b $P < 0.05$, vs the preoperative period.

DISCUSSION

Laparoscopic cholecystectomy is becoming the choice of surgery for uncomplicated cholelithiasis because it had induced less tissue trauma response throughout the course of wound healing compared to open cholecystectomy. Surgery stimulates a series of hormonal and metabolic changes that constitute the stress response. Surgery also induces neurohormonal events that include activation of sympathetic nervous system and stimulation of hypothalamic-pituitary-adrenal axis initially. Then the adrenal cortex is activated, promoting the release of neurohormonal transmitters that would influence the intensity of postoperative pain and duration of postoperative ileus^[5-7]. ACTH, catecholamine, cortisol, and glucagon all played crucial roles in the mediation of stress response. In response to sepsis and trauma, massive catecholamine, cortisol, and glucagons are released, while serum insulin concentrations decrease relatively, and decrease of insulin levels is in correlation with the severity of the sepsis and trauma^[8-12]. In the present study, we found a marked decrease of insulin levels from baseline in OC group on the 3rd postoperative day, while the intergroup difference was not significant on either 1st or 3rd postoperative day. GH and cortisol levels increased from baseline in both groups on the 1st and 3rd postoperative day, and there was a more marked increase in OC group. On the 1st postoperative day GH and cortisol concentrations were both higher in OC than those in LC group.

The cytokines and CRP were objective markers of operative stress response as well as the mediators of host immunologic reaction. Derived from immune system or other tissues, TNF, IL-1 and IL-6 were the major mediators of the acute-phase response^[13-15]. In a recent study, Bruce and coworkers^[16] examined the changes of CRP, IL-1 Ra, IL-6, and TNF- α in LC and OC patients after surgery. A marked and persistent raise of IL-6 levels was detected from 8 hours to 7 days postoperatively in OC group, while the concentrations of CRP and albumin were comparable in the two groups. IL-1ra levels were significantly raised as early as 4 hours following incision in OC group, compared to LC group. IL-6 levels rose significantly and early (1 hour) in both groups, but there was a more prominent and prolonged response in patients undergoing OC. Significant intergroup difference of IL-6 levels was present as early as 8 hours following incision^[17-21]. In our study, we found that CRP levels rose significantly from baseline on both day 1 and day 3 after surgery in the two groups, but more prominently in OC group.

In response to the surgical trauma, the body usually presents with a hyper-metabolic state. Such a state is directly linked to the activation of sympathetic nervous system, the increase of oxygen and energy consumption, the negative nitrogen balance, and the synthesis of CRP. All surgical traumas will induce neuroendocrine activation and protein catabolism, and the nitrogen excretion is therefore increased (mainly as BUN, sometimes as SCr)^[22,23]. The amount of the increased nitrogen excretion was determined by the extent of stress, which is proportional to the intensity of injury response. Thus, the degree of metabolic restoration could be acquired using systemic nitrogen balance measurements^[8]. To our knowledge, this study is the first to assess the effect of mini-invasive surgery on body REE consumption. In the study, we observed the perioperative changes of REE levels of LC and OC groups using indirect calorimeter. As the result, REE increased significantly (165.3 Kcal) from baseline in the 1st postoperative day in OC group, while on the 3rd day the elevation was not significant (57.3 Kcal). The LC group also revealed marked increase (60.1 Kcal) in the 1st postoperative day, but not in the 3rd day. The intergroup difference of REE levels was significant (with higher levels in OC group) at all phases postoperatively. RQ decreased significantly on the 1st

postoperative day in both groups. Thus, our study revealed that LC was less invasive and induced less host stress response and metabolic disturbance compared with traditional OC and it therefore might be more beneficial to the restoration of nitrogen balance and metabolism.

During LC, pneumoperitoneum is induced by insufflation of carbon dioxide, which may be accompanied with disturbance of acid-base balance and pulmonary perfusion^[24-27]. Open surgery, on the other hand, usually results in pulmonary dysfunction. Previous studies have shown that on the 1st postoperative day, FVC and FEV1 decreased 40-70 % in patients undergoing OC, compared to 20-40 % in patients undergoing LC. There are possibly two explanations for this. One is that postoperative wound pain often causes shallow respiration, which may lead to small bronchiole closure, the pulmonary blood shunt, and hence the hyponoxia. Increased oxygen consumption after surgery may be another explanation^[28-31]. In this study, we observed that artery oxygen consumption fell significantly from baseline on day 1 and restored to preoperative levels on the day 3 postoperatively in LC patients, with no significant reduction in OC patients. SO₂ decreased significantly on the 1st postoperative day on both groups, and on the 3rd postoperative day it was higher in LC group than in OC group. Penumoperitonium could explain the reduced oxygen supply at early postoperative phases in LC patients. However, the influence of wound pain on respiration is more pronounced and permanent OC than in LC patients, this may be the reason why the intergroup difference is significant on the 3rd postoperative day. HCO₃ and BE raised significantly from baseline in OC group on the 3rd postoperative day, and BE was significantly higher in LC group than that in OC group on the day. PH levels were much lower in LC group than those in OC group on the 1st postoperative day. This is possibly because of the postoperative acidemia elicited by the retention of CO₂ during pneumoperitonium. Much attention should be paid to this change during LC.

In conclusion, LC results in less prominent stress response and metabolic interference compared to open surgery. These advantages are beneficial to the restoration of stress hormones, the nitrogen balance, and the energy metabolism. However, LC can also induce acidemia and pulmonary hypoperfusion because of the pneumoperitonium it uses during surgery.

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