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Comparison of the stress response after laparoscopic and open cholecystectomy

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Abstract
Background: We designed a prospective controlled animal study to compare the stress response induced after laparoscopic and open cholecystectomy.
Methods: Twelve female pigs (20–25 kg body weight) were anesthetized with ketamine, pentobarbital, and fentanyl. The animals were randomized into the following four groups: control (C), pneumoperitoneum with CO_2 at 14–15 mmHg (P), laparoscopic cholecystectomy (LC), and open cholecystectomy (OC). The average duration of the procedure in each group was 35 min.
Results: Central venous pressure, mean arterial pressure, pulmonary capillary wedge pressure, and cardiac output were monitored. Measurements were recorded when animals were anesthetized (baseline), immediately before and after surgery, and thereafter every 30 min for a maximum of 3 h. White blood cell count (WBC) was determined from blood samples taken before and after 3 h of surgery. Ultrasound-guided liver biopsies were done preoperatively and after 3 h of surgery. Total RNA was isolated from the liver biopsy specimens. Steady-state mRNA levels of β-fibrinogen (β-fib), α 1-chymotrypsin inhibitor (α1-CTI), metallothionein (MT), heat shock protein 70 (Hsp70), and polyubiquitin (Ub) were detected by Northern blot/hybridization. There were no statistical differences in the hemodynamic parameters among the groups. The number of circulating neutrophils and monocytes decreased only after LC. Expression of Hsp70 was not induced after any surgical procedure, and the mRNA levels of Ub did not change after surgery. The expression of α1-CTI and β-fib (acute phase genes) were similarly increased after LC and OC. Steady-state mRNA levels of MT were slightly increased after P and LC but not after OC.
Conclusion: These data indicate that there are no significant differences between LC and OC in terms of induction of the stress response.

Key words: Acute phase — Cholecystectomy — Gene expression — Inflammation — Laparoscopy — Stress

Now that laparoscopic cholecystectomy (LC) has gained clinical acceptance, it is considered the gold standard for the treatment of symptomatic cholelithiasis [9, 20]. The major advantages of the laparoscopic procedure over conventional open cholecystectomy (OC) are reduced hospitalization time, earlier return to normal activity, improved cosmetic results, less postoperative morbidity [9], and reduced impairment of the immune system [10, 17]. However, there is still some controversy about the relative levels of stress induced by the laparoscopic and traditional procedures [16, 18].

Although it is generally believed that laparoscopic procedures incur less stress due to the smaller size of the surgical wound and less tissue manipulation, the stress response induced by the various components of the laparoscopic procedure, including pneumoperitoneum, type of gas used for insufflation, and longer operating time, has not yet been evaluated. The hemodynamic and metabolic responses, such as increase in levels of ACTH, cortisol, glucose, lactate, prolactin, and decrease of albumin, have been found to be identical after LC and OC [15, 21]. These results suggest that the metabolic response is similar for both operative techniques. Others studies have shown a significant increase in the plasma levels of C-reactive protein (CRP), interleukin-6 (IL-6), and prolactin following conventional OC as compared to LC [4, 12, 16]. These observations suggest that there is a difference in the inflammatory response associated with these two procedures.

The present study used a porcine model to compare the

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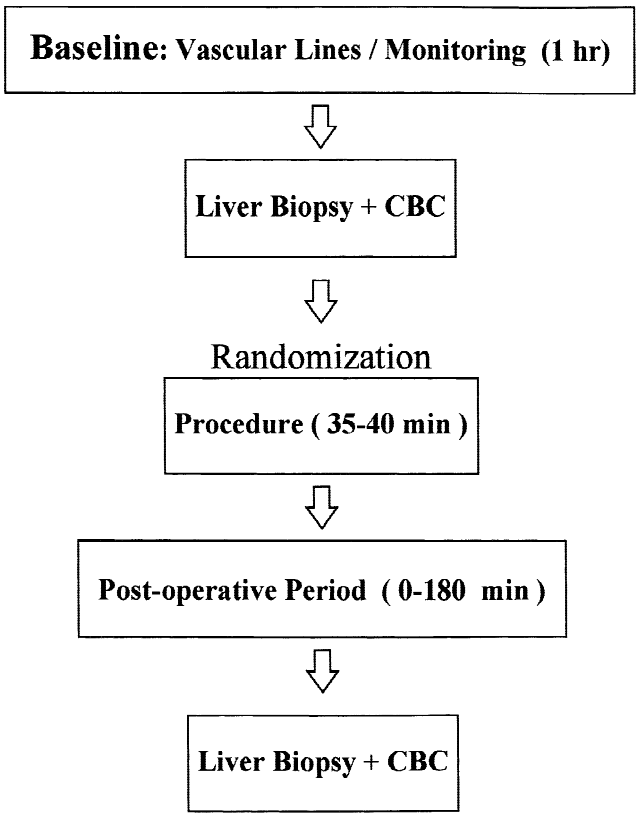

Fig. 1. Experimental protocol. CBC, complete blood cell count.

stress response at the physiological and molecular level following laparoscopic and conventional cholecystectomy.

Materials and methods

Twelve female pigs (20–25 kg) were initially anesthetized with ketamine (15 mg/kg, IM) and maintained under anesthesia with bolus intravenous injection of pentobarbital (30 mg/kg) and continuous infusion of fentanyl (2 mg/kg/h). The animals were paralyzed with a continuous infusion of pancuronium (0.2 mg/kg/h) and ventilated with a mechanical ventilator (Dual Phase Control Respirator Pump, Model 613; Harvard Apparatus, South Natick, MA, USA) via an oral cuffed endotracheal tube. Body temperature was kept at 37–37.5°C with a heating pad. Lactated Ringer's solution was infused intravenously at a rate of 10 ml/kg/h. The animals received nearly 100% oxygen through a 10 L/min flow for the duration of the experiment.

The following parameters were monitored during the surgery: (a) mean arterial pressure via the left carotid artery with the catheter tip in the thoracic aorta (16-gauge silicone rubber); (b) pulmonary artery pressure, pulmonary capillary wedge pressure, and cardiac output via a thermodilution catheter placed through the left internal jugular vein (5F balloon-tipped pulmonary artery catheter); (c) central venous pressure with the catheter tip in the right atrium (5F balloon-tipped pulmonary artery catheter). All transducers (Statham P23dB; Statham Instruments) were connected to a Grass 7-D polygraph for continuous data collection of central venous pressure (CVP), pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), and mean arterial pressure (MAP). PCWP and cardiac output (CO) were measured with Swan-Ganz thermodilution catheters (Cardiac Output Computer, 9520A; Edward Laboratories, Santa Ana, CA, USA). Data were collected continuously and recorded at baseline, immediately before and after the operative procedure, and thereafter every 30 min for 180 min. The experimental sequence is shown in Fig. 1. The animals were monitored for 15 min (baseline) after placement of the monitoring lines. At the end of this phase, an ultrasound-guided percutaneous liver biopsy was done.

The pigs were then randomized into four groups. The pigs in group 1 (C) were kept anesthetized for 215 min as controls. In group 2 (P), a Veress needle was inserted using standard techniques and the abdomen was insufflated with carbon dioxide (CO_2) to a pressure of 14–15 mmHg (Olympus insufflator) for 35 min. In group 3 (LC), a Veress needle was inserted using standard techniques and the abdomen was insufflated with CO_2 to a pressure of 14–15 mmHg. Two 10–12-mm trocars and two 5-mm trocars (Ethicon) were then placed in a standard array for a laparoscopic cholecystectomy, and the gallbladder was removed using standard techniques. All the laparoscopic procedures were performed using disposable laparoscopic instrumentation (Ethicon) and a 30° telescope (Storz) for visualization. In group 4 (OC), a conventional open cholecystectomy was performed through a right subcostal abdominal incision.

The average duration of the surgical interventions was 35 min. After the surgical procedure, all animals were monitored for another 180 min. Data were recorded every 30 min. Finally, ultrasound-guided liver biopsies were again done. A complete blood cell count, including leucocytes (WBC), neutrophils, lymphocytes, eosinophils, hemoglobin (HGB), hematocrit (HCT), and platelets (PLT), was done before and 3 h after the operation. The animals were located according to a protocol approved by the Animal Care and Use Committee of the Johns Hopkins University.

Isolation of RNA and Northern blot analysis

Liver samples were obtained through ultrasound-guided liver biopsies using a Tru-Cut biopsy needle (Baxter Healthcare Corporation, Deerfield, IL, USA). Total RNA was isolated from the liver samples as described by Chomczynski and Sacchi [5]. RNA samples (10 μg) were electrophoresed in formaldehyde-agarose gels. RNA patterns were visualized by staining of the gel with ethidium bromide. RNA was transferred onto nylon modified membranes (GeneScreen Plus; NEN Research Products, Boston, MA, USA) by capillary action. Blots were stained with methylene blue (0.03%) in 3M NaOAc, pH 5.2, prior to hybridization, and the signal corresponding to the 18S rRNA was determined using a laser-scanning densitometer (Molecular Dynamics). Blots were hybridized with the following radiolabeled cDNAs probes: heat shock protein 70 (Hsp70, pig, full length), α-fibrinogen (α-fib, pig, fragment), metallothionein (MT, pig liver, full length), α_1-chymotrypsin inhibitor (α_1-CTI, pig, full length), and polyubiquitin (Ub, pig, fragment) [3].

The cDNA probes were radiolabeled by the random primer method [8] using [α-32P]dATP and [α-32P]dCTP (ICN Pharmaceuticals, Irvine, CA, USA) as previously described [2]. Blots were hybridized in 50% formamide, 75 mM sodium citrate (pH 7.0), 0.75 M NaCl, 1% sodium dodecyl sulfate (SDS), 2.5× Denhardt's solution, 100 g/ml denatured salmon sperm DNA, 1 mM EDTA, and 20 mM sodium phosphate (pH 6.5) for 16 h at 42°C. Blots were washed with [50 mM tris (hydroxymethyl)aminomethane (Tris pH 8.6), 1 M NaCl, 2 mM EDTA, and 1% SDS] at 42°C for ≥2 h, with a minimum of six changes. Later, blots were washed with 2× saline-sodium citrate (SSC) buffer [0.015 M sodium citrate (pH 7.0)–0.15 M NaCl] containing 0.1% SDS at 42°C for 30 min and 2× SSC–0.1% SDS at 65°C for 5 min.

Blots were then exposed to x-ray film (Kodak) at–70°C in the presence of intensifying screens. Autoradiograms in the linear range of exposure were quantitated by laser-scanning densitometry. The signal intensity of the respective mRNA was normalized by the signal correspondent to the 18S rRNA. The latter is an indirect measurement of the total RNA loaded in the respective lane of the gel.

Statistical analysis

Hemodynamic data were recorded at baseline, immediately pre- and postoperatively, and thereafter every 30 min for 180 min. For general significance between and within groups, a one-way analysis of variance (ANOVA) test was performed. To elucidate the specific significances between groups, a multiple pairwise comparison test was performed (Dunnett's method). Comparison of blood cell count within each group was performed using Student's *t*-test. Differences were considered significant when p value was < 0.05. Data were expressed as mean ± standard error of the mean (SEM).

Results

Twelve pigs were included in this study. The average weight of the animals was 20.7 ± 1.1 kg in the control

Table 1. Changes in mean arterial pressure (MAP)

			Postoperative						
MAP	Baseline	Preoperative	0 min	30 min	60 min	90 min	120 min	150 min	180 min
Control	99 ± 10	92 ± 22	97 ± 24	97 ± 12	105 ± 16	107 ± 25	112 ± 23	113 ± 26	112 ± 24
Pneumoperitoneum	92 ± 6	87 ± 7	90 ± 10	99 ± 4.7	103 ± 7	113 ± 3	114 ± 5	113 ± 1	118 ± 1 [a]
LC	123 ± 9	149.3 ± 22	113 ± 2.7	100 ± 12	129 ± 3	129 ± 3	127 ± 1	134 ± 1	121 ± 10
OC	95 ± 8	88 ± 6	88 ± 12	104 ± 17	104 ± 18	112 ± 10	105 ± 20	112 ± 7	116 ± 12

Data are mean ± SEM; $n = 3$ for each group
[a] $p < 0.05$ vs preoperative one-way ANOVA + Dunnet's method

group, 21.6 ± 2.0 kg in the pneumoperitoneum group, 21.7 ± 1.1 kg in the LC group, and 21.7 ± 0.8 kg in the OC group. The total amount of IV fluid infused in the animals during the study was 726 ± 39 ml in the control group, 750 ± 72 ml in the pneumoperitoneum group, 761 ± 39 ml in the LC group, and 761 ± 30 ml in the OC group. No statistically significant differences were found in the operative time between LC and OC groups (35 ± 5 min vs 40 ± 5 min, respectively).

Changes in hemodynamics after LC and OC

Hemodynamic parameters (MAP, CVP, PAP, PCWP, CO) were monitored and recorded at baseline, immediately before and after the operative procedure, and thereafter every 30 min for 180 min. There were no statistical differences in these hemodynamic parameters before or after the operative procedures in any group (Tables 1–5). There was a statistically significant increase over preoperative values in MAP ($p = 0.008$) only in the P group at 180 min following the release of the pneumoperitoneum.

Complete blood cell count after LC and OC

Samples for complete blood cell count (CBC) were drawn before and 180 min after the procedure to estimate the degree of bleeding secondary to the surgical procedure and variations in the number of leucocytes. CBC showed no statistically significant differences in postoperative HGB, HCT, PLT as compared to preoperative values in any group. However, there was a statistically significant decrease in postoperative WBC in the LC group ($p = 0.02$). This drop in WBC corresponded to a decrease in neutrophil and monocyte counts and was not observed in any other group. There was a statistically significant increase in monocyte count following OC (Table 6).

Gene expression after LC and OC

Steady-state mRNA levels of different genes involved in the stress response were evaluated in total RNA samples isolated from liver biopsy specimens obtained before and after LC and OC (Table 7). Two acute phase genes, α-CTI and α-fib, were analyzed. There was a threefold increase in α-CTI mRNA levels following LC and a 2.4-fold increase following OC. These observations are in contrast with an increase of 1.3- and 1.5-fold in the C and P groups, respectively (Fig. 2A,B). There was also an increase of 2.3-fold in α-fib mRNA levels following LC and a threefold increase following OC. The C and P groups showed a 1.6- and a 1.5-fold increase, respectively (Fig. 3A,B). There was a 1.8-fold increase in MT mRNA level in the LC and P groups, whereas no apparent changes were observed in the C and OC groups (Fig. 3a,c).

The expression of two heat shock proteins, Hsp70 and Ub, were also evaluated. No detectable mRNA level of Hsp70 was observed after any procedure. Moreover, there was no change in Ub mRNA levels before and after surgery in any group (data not shown).

Discussion

The clinical benefits of LC over OC are well documented. These include less hospital time, earlier return to normal activity, better cosmetic results, and reduced postoperative morbidity [9, 20]. In addition, the immune system seems to be significantly less impaired following LC [10, 17]. These benefits are in part due to a reduction in surgical wounding and tissue manipulation. However, we know far less about the stress response produced by the different interacting factors involved in the laparoscopic procedure, such as the pneumoperitoneum, the type of gas used for the insufflation, and the longer operative time [11, 18]. In the present study, the stress exerted by a well-accepted laparoscopic procedure, cholecystectomy, was compared with the equivalent open operative procedure. The stress response was evaluated at the molecular and physiological level.

LC and OC were performed in anesthetized pigs, and different hemodynamic parameters were evaluated before and after surgery. There were no statistically significant differences in MAP, CVP, PAP, PCWP, or CO between the LC and OC subjects during the postoperative recovery period. These results suggest that there are no hemodynamic differences between the two types of surgery during postoperative recovery. These results resemble those reported in previous studies that measured similar parameters during LC and OC. These studies showed that transient adverse hemodynamic effects—such as an increase in MAP, CVP, systemic vascular resistance, and heart rate, as well as a decrease in stroke volume, cardiac index, and CO—return to normal levels immediately after the release of pneumoperitoneum during LC [11, 14, 18]. However, it is still unclear whether these effects are the result of the pneumoperitoneum itself or the consequence of the peritoneal absorption of CO_2.

Table 2. Changes in central venous pressure (CVP)

			Postoperative						
CVP	Baseline	Preoperative	0 min	30 min	60 min	90 min	120 min	150 min	180 min
Control	14 ± 1	15 ± 1	13 ± 1.5	14 ± 2.2	15 ± 3.2	14 ± 2	14 ± 2	15 ± 3	15 ± 2.5
Pneumoperitoneum	14 ± 0.6	15 ± 0.3	16 ± 0.3	15 ± 0.3	16 ± 0	16 ± 0	16 ± 0.1	16 ± 0.1	16 ± 0
LC	12.7 ± 1.3	10.7 ± 3	15 ± 4.6	12 ± 2.5	13 ± 2.4	13 ± 1.8	13 ± 1.8	13 ± 2	12 ± 1.5
OC	11.7 ± 0.9	15 ± 2.4	16 ± 2.2	15 ± 2.6	15 ± 1.5	18 ± 5	18 ± 6.9	17 ± 3.5	15 ± 2.3

Data are mean ± SEM; $n = 3$ for each group

Table 3. Changes in pulmonary artery pressure (PAP)

			Postoperative						
PAP	Baseline	Preoperative	0 min	30 min	60 min	90 min	120 min	150 min	180 min
Control	22 ± 1.2	23 ± 2.5	21 ± 1.5	23 ± 3.7	23 ± 3.1	24 ± 4.3	22 ± 2.8	24 ± 4.2	22 ± 2.3
Pneumoperitoneum	23 ± 1	27 ± 4.2	25 ± 2	25 ± 2.1	25 ± 3	27 ± 3.5	27 ± 3	25 ± 1.7	26 ± 2.3
LC	26 ± 1	23 ± 1	25 ± 3.3	26 ± 2.3	27 ± 4.7	27 ± 2.7	29 ± 3.8	27 ± 1.5	26 ± 2.7
OC	23 ± 0.7	22 ± 0.7	23 ± 1.2	23 ± 1	25 ± 1.5	24 ± 1	29 ± 4.2	27 ± 3	25 ± 1.2

Data are mean ± SEM; $n = 3$ for each group

Table 4. Charges in pulmonary capillary wedge pressure (PCWP)

			Postoperative						
PCWP	Baseline	Preoperative	0 min	30 min	60 min	90 min	120 min	150 min	180 min
Control	15 ± 0.3	15 ± 0.3	14 ± 0.6	15 ± 1.2	14 ± 0.9	15 ± 1.2	14 ± 0.6	15 ± 0.6	15 ± 0.9
Pneumoperitoneum	14 ± 0.3	16 ± 1	14 ± 0.3	14 ± 0.7	14 ± 0.6	14 ± 0.7	14 ± 0.6	14.3 ± 0.3	14 ± 0.9
LC	15 ± 2.4	15 ± 1	16.7 ± 2.6	17 ± 1.5	17 ± 2.5	18 ± 3.5	18 ± 1.5	21 ± 0.9	17 ± 3.5
OC	13.7 ± 1	14 ± 1.5	13.7 ± 0.7	14 ± 1.3	15 ± 1.9	15 ± 1.3	15 ± 2.3	15 ± 0.9	15 ± 0.9

Data are mean ± SEM; $n = 3$ for each group

Table 5. Changes in cardiac output (CO)

			Postoperative						
CO	Baseline	Preoperative	0 min	30 min	60 min	90 min	120 min	150 min	180 min
Control	2.1 ± 0.5	1.9 ± 0.4	2 ± 0.4	2.1 ± 0.3	2.2 ± 0.1	2.5 ± 0.5	2.7 ± 0.1	2.5 ± 0.4	2.3 ± 0.4
Pneumoperitoneum	4.5 ± 0.7	3.9 ± 0.4	4.5 ± 0.8	4 ± 0.4	4.2 ± 0.5	4.6 ± 0.8	4.3 ± 0.7	3.9 ± 0.6	4.5 ± 0.8
LC	4.8 ± 0.4	3.9 ± 0.6	4.3 ± 0.9	3.5 ± 0.3	3.7 ± 0.4	3.2 ± 0.2	3.3 ± 0	3 ± 0	2.9 ± 0.1
OC	2.6 ± 0.2	3.5 ± 0.6	3.2 ± 0.1	3.3 ± 0.5	2.9 ± 0.2	3.1 ± 0.4	2.9 ± 0.2	3 ± 0.7	2.9 ± 0.2

Data are mean ± SEM; $n = 3$ for each group

Table 6. Complete blood count CBC value

CBC		1. Control		2. Pneumoperitoneum		3. LC		4. OC	
Parameters	Normal values	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op
HGB	10–16 g/dl	9.9 ± 0.6	9.1 ± 0.1	9.5 ± 0.2	8.7 ± 0.2	11.3 ± 1	10.6 ± 0.7	10.7 ± 0.7	9.7 ± 0.1
HCT	32–50%	67.8 ± 8	64.7 ± 10	42.6 ± 1	39.8 ± 1	50.7 ± 5	47.4 ± 3	50.4 ± 4	45.4 ± 1
PLT	250–850 k/μl	1122 ± 352	1054 ± 376	731 ± 53	610 ± 23	533 ± 28	595 ± 83	601 ± 107	548 ± 120
WBC	6–17 k/μl	12.9 ± 4.3	10.9 ± 1.8	15.1 ± 1.5	19.8 ± 3.9	18.6 ± 1.8	10.2 ± 1.4[a]	14.4 ± 3.3	16.2 ± 4
Lymphocytes	0.6–3.4 k/μl	4.8 ± 1.3	5.3 ± 2.1	7.2 ± 3.2	5.8 ± 1.7	2.4 ± 0.6	3.9 ± 1.2	7.4 ± 3.1	2.7 ± 0.5
Neutrophils	2–6.90 k/μl	7 ± 4.7	4.7 ± 1.8	5.9 ± 1.5	11.9 ± 4.6	14.4 ± 2.4	5.5 ± 1.2[a]	5.9 ± 2.1	11.1 ± 4
Eosinophils	0–0.7 k/μl	0.1 ± 0	0.1 ± 0	0.1 ± 0	0 ± 0	0 ± 0	0.1 ± 0	0.1 ± 0	0.1 ± 0
Monocytes	0–0.9 k/μl	1.1 ± 0.2	0.9 ± 0.5	2 ± 0.3	2 ± 0.4	1.7 ± 0.1	0.7 ± 0.2[a]	0.8 ± 0.1	2.36 ± 0.4[a]

HGB, hemoglobin; HCT, hematocrit; PLT, platelets; WBC, white blood cells
Data are mean ± SEM; $n = 3$ for each group
[a] $p < 0.05$ vs preoperative by *t*-test

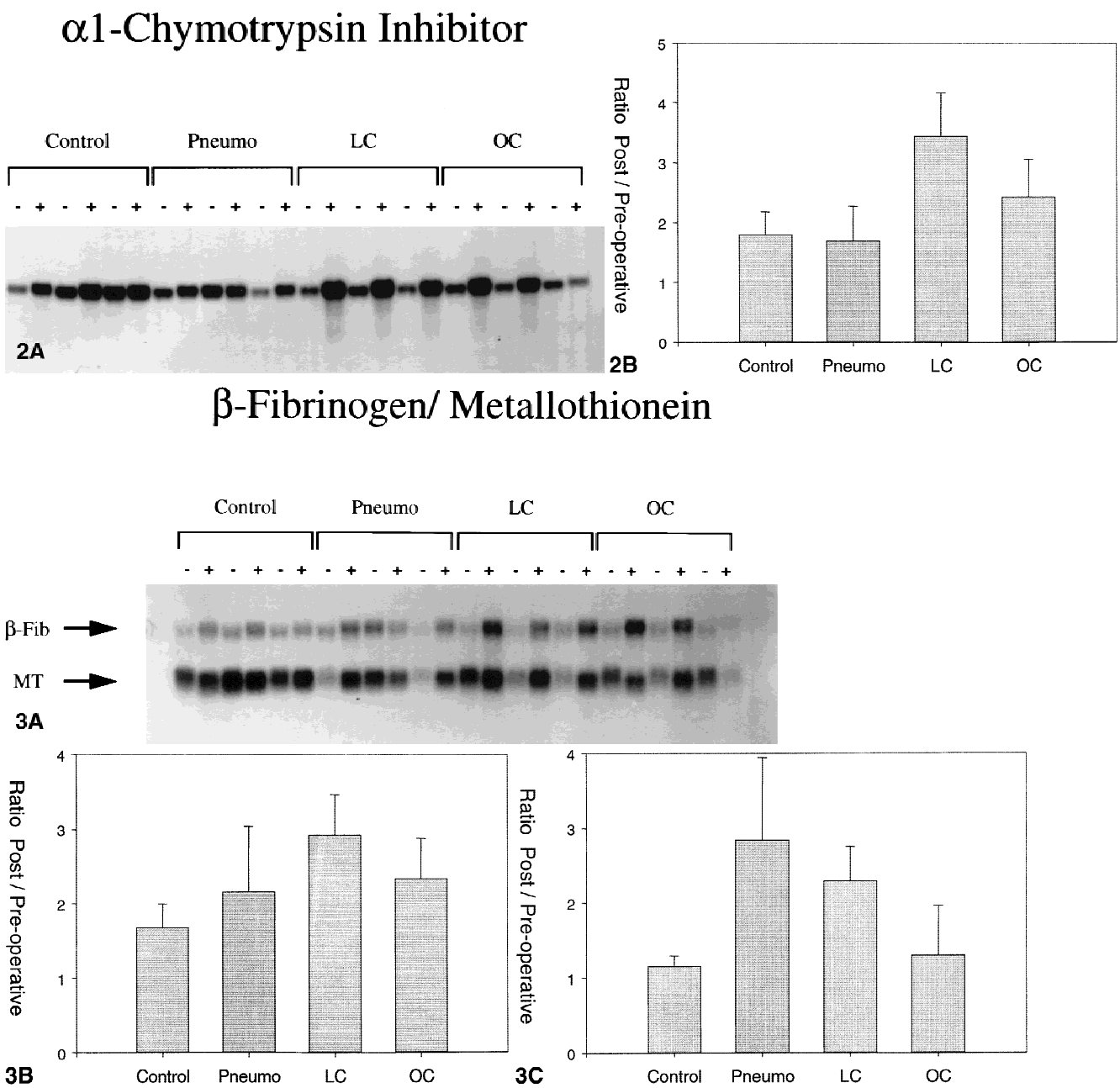

Fig. 2. Percutaneous liver biopsies were done before and 180 min after the operative procedure to analyze α_1-chymotrypsin inhibitor mRNA expression using Northern blot/hybridization techniques. There was a threefold increase in α_1-CMI mRNA levels following LC and a 2.4-fold increase following OC. Control group and pneumo group showed a 1.3- and 1.5-fold increase, respectively. **A** Pneumo = pneumoperitoneum group; LC = laparoscopic cholecystectomy group; OC = open cholecystectomy group-.–preoperative mRNA levels. + postoperative mRNA levels. **B** Ratio of postoperative/preoperative. Data are expressed as percent of increase (mean ± SEM); n = 3 for each group.

Fig. 3. Percutaneous liver biopsies were done before and 180 min after the operative procedure to analyze β-fibrinogen and metallothionein mRNA expression using Northern blot/hybridization techniques. There was a 2.3-fold increase in β-fib mRNA levels following LC and a threefold increase following OC. There was a 1.8-fold increase in the mRNA expression of MT in both the pneumoperitoneum group and the LC group. There were minimal changes in MT mRNA expression in the control group and the OC group. **A** Pneumo = pneumoperitoneum group; LC = laparoscopic cholecystectomy group; OC = open cholecystectomy group.–preoperative mRNA levels. + postoperative mRNA levels. **B, C** Ratio of postoperative/preoperative. Data are expressed as percent of increase (mean ± SEM); *n* = 3 for each group.

Previous studies have found no statistically significant differences in serum levels of cortisol, glucose, albumin, and catecholamines following LC or OC [11]. However, these metabolic parameters returned to normal values more rapidly after LC than after OC [15, 16]. Recent studies have shown a higher elevation of CRP (an acute phase protein) and IL-6 (a cytokine) plasma levels with OC than with LC [4, 12, 21].

We measured the expression level of different genes involved in the stress response after OC and LC. There was no induction in the expression of the major heat shock protein, Hsp70, following either LC or OC. Another heat shock

protein, polyubiquitin, which is involved in cytosolic protein degradation [6], showed no change in expression during any of the protocols. These findings suggest that one of the most primitive mechanisms of cellular defense, the heat shock response, is not triggered in the liver by either conventional or laparoscopy cholecystectomy. In contrast, the mRNA levels of the acute phase genes α_1-CTI and β-fib were both increased after LC and OC. However, there were no differences in the level of induction of these genes after either type of surgery. These observations indicate that activation of the systemic host defense system is equal after both procedures. The data suggest that there are no differences in the inflammatory response, at least at the level of the acute phase response. The expression of MT, which has been observed to parallel the acute phase response in the liver [13], seems to increase slightly during LC and P compared to OC. This observation is particularly interesting since MT is an oxygen radical and metal scavenger. Thus, its expression may be directly related to the effect of the CO_2 used during the laparoscopic procedure. More studies are required to substantiate this hypothesis.

It is particularly interesting to note that whereas the WBC decreased after LC, an increase was observed after OC. Analysis of the cell population indicated that this difference can be traced to a decrease in the number of neutrophils and monocytes in circulation after LC as opposed to the increase seen with OC. Under certain conditions there are cytokines, such as IL-8, that emerge from the injured local tissue; these cytokines are highly chemotactic for neutrophils and monocytes [1]. Thus, it is possible that the decrease in circulating neutrophils and monocytes is secondary to their sequestration in different organ systems. For example, it is well established that in animals in which the inflammatory response is induced by intravenous administration of bacterial endotoxin, there is infiltration of leukocytes in the liver and lung [19]. In contrast, we observed an increase in the level of neutrophils and monocytes in circulation after OC. An increase in the number of neutrophils has also been reported in human patients after OC [17]. These findings may suggest a greater magnitude of inflammatory response following OC. Dionigi et al. have also reported a transient decrease, lasting for ≤7 days, in levels of circulating CD3 cells and OKDR lymphocytes following OC when compared to LC [7]. Our data suggest that OC is followed by significant depression of circulating lymphocytes, whereas LC induces a progressive increase in these cells.

In summary, our study indicates that the level of stress induced by LC is equivalent to or less than that associated with OC. Furthermore, the results suggest that the clinical advantages of LC over OC are due not to a reduction in operative stress but rather to a more rapid recovery, possibly as a result of less postoperative pain and fatigue.

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