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Acute Phase is the Only Significantly Reduced Component of the Injury Response after Laparoscopic Cholecystectomy

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Abstract. The objective demonstration of improved postoperative recovery suggests that the surgical injury response induced by the laparoscopic approach is less intense than that after open surgery. Twenty-five patients diagnosed as having noncomplicated gallstones were studied prospectively. They were operated by laparoscopy (group I, $n = 12$) or open surgery (group II, $n = 13$). Analgesia requirements ($p < 0.026$) and postoperative stay ($p < 0.001$) were significantly less in group I. Cholecystectomy performed by either technical options induced a significant increase over basal values of glucose, lactate, white blood cell count, prolactin, ACTH, cortisol, interleukin 6, C-reactive protein, and PCO_2. Both surgical procedures induced a significant reduction of total proteins, albumin, prealbumin, free fatty acids hemoglobin, hematocrit, and pH. There were no differences between the levels of growth hormone, insulin, glucagon, or PO_2 during any of the periods studied. Comparison of the results of the two cholecystectomy techniques showed that laparoscopic cholecystectomy induced a significantly less intense acute-phase response (area under the curve) of interleukin 6 (17 ± 17 versus 47 ± 26 pg/ml × hr × 10^2; $p < 0.003$), C-reactive protein (16 ± 12 versus 35 ± 16 mg/dl × hr × 10; $p < 0.004$), and prealbumin (16 ± 2.7 versus 13.8 ± 2.3 mg/dl × hr × 10^2; $p < 0.05$). The surgical injury response after laparoscopic cholecystectomy is similar to that after open cholecystectomy, but the acute-phase response component is less intense. This finding may be a consequence of the reduced size of the operative wound with laparoscopic cholecystectomy.

Laparoscopic cholecystectomy has become the procedure of choice for the treatment of gallstones [1, 2]. The most important advantage of laparoscopic surgery is the rapid, smooth recovery of the patient, with a shorter duration of postoperative ileus, less requirement for analgesia, and less disturbance of respiratory function. All these features shorten the hospital stay and convalescence period [3].

It is well demonstrated that the controlled injury caused by a surgical operation is followed by a characteristic period of biologic repair with neuroendocrine, acute-phase, metabolic, and immunologic responses [4–7]. The intensity of this combined response can be measured via analysis of several clinical, biochemical, or hormonal parameters [4–7]. The objective demonstration of improved postoperative recovery suggests that operative trauma and the concomitant response to surgical injury after the laparoscopic approach are less intense than after open surgery.

Several studies have analyzed the surgical stress and biologic response induced by laparoscopic cholecystectomy compared with the open approach, but the results are contradictory, and no agreement has been forthcoming [8–20] (Table 1). The aim of this study was to investigate the response to injury induced by two surgical models (laparoscopic versus open cholecystectomy) by evaluating three of its components (neuroendocrine, acute phase, and metabolic).

Material and Methods

Twenty-five patients diagnosed as having noncomplicated gallstones were included prospectively in this study. All presented a low surgical risk (ASA I or II). No patient was receiving long-term drug therapy. The patients underwent laparoscopic cholecystectomy (group I, CxL; $n = 12$) or open surgery (group II, CxO; $n = 13$) according to the availability of laparoscopic equipment in the operating theater.

The patients received 10 mg of diazepam the previous night and 2 hours before anesthesia. All patients received general anesthesia with orotracheal intubation: thiopental (5 mg/kg) or propofol (0.2 mg/kg) for induction and isofluorane (0.5–1.0%) or fentanyl (15 mg/kg) for maintenance. The muscular blockade was obtained with atracurium besylate in continuous perfusion. The CO_2 level was monitored throughout the operation with a capnograph.

In group I laparoscopic cholecystectomy was performed following the technique proposed by Reddick and Olsen [21] with four trocars (two of 5 mm diameter and two 10 mm diameter). Intraabdominal CO_2 pressure was maintained at 12 to 14 mmHg. Intraoperative cholangiography was attempted in all cases. In group II cholecystectomy was performed through a subcostal incision of 8 to 10 cm. A cholangiogram was obtained in all cases.

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Table 1. Response to surgical injury induced by laparoscopic versus open cholecystectomy.

First author	Year	Catecholamines	ACTH	Cortisol	Glucose	WBCs	IL-6	CRP
Mealy [9]	1992	↑ CxL	—	—	—	—	—	↓ CxL
Joris [13]	1992	=CxL	—	=CxL	↓ CxL	↓ CxL	↓ CxL	↓ CxL
Roumen [15]	1992	—	—	↓ CxL	—	—	—	↓ CxL
Jakeways [10]	1994	—	—	=CxL	↓ CxL	—	↓ CxL	↓ CxL
Dietrich [11]	1992	—	↑ CxL	↑ CxL	—	—	—	↓ CxL
McMahon [12]	1993	—	—	=CxL	—	—	=CxL	=CxL
Papalois [14]	1993	—	—	↓ CxL	—	—	—	—
Berggren [18]	1994	=CxL	—	=CxL	=CxL	=CxL	=CxL	=CxL
Vander Velpen [17]	1994	—	—	—	—	—	=CxL	—
Dionigi [19]	1994	—	↓ CxL	↓ CxL	—	—	—	↓ CxL
Targarona (present study)	1994	—	=CxL	=CxL	=CxL	=CxL	↓ CxL	↓ CxL

CxL: laparoscopic cholecystectomy; CRP: C-reactive protein; WBCs: white blood cells; IL-6: interleukin 6; ↑: significant increase; ↓: significant decrease; =: no difference.

Table 2. Parameters evaluated.

Neuroendocrine response
ACTH
Cortisol
Prolactin
Growth hormone
Acute-phase response
Interleukin 6
C-reactive protein
Prealbumin
Metabolic response to injury
Insulin
Glucagon
Glucose metabolism
Glucose
Lactate
Protein metabolism
Total proteins
Albumin
Lipid metabolism
Triglycerides
Free fatty acids
Blood gases and pH
pH
PCO_2
PO_2
Hematologic parameters
Hematocrit
Hemoglobin
Leukocyte count

All patients received the same regimen of intravenous fluids (5% glucose and Ringer's lactate 3000 ml/24 hr) until the beginning of oral intake. A postoperative analgesia regimen was established at free demand with ketorolac.

Age, sex, weight, height, ASA type, analgesia requirements, hospital stay, morbidity, and mortality were recorded in all cases. Venous and arterial blood samples were obtained preoperatively and at 1, 24, and 72 hours after surgery. The parameters measured are listed in Table 2.

Methods of Analysis

Neuroendocrine Response. Serum ACTH was measured by radioimmunoassay (RIA) (Allégro, H-ACTH, Kit 40-2194: Nichols Institute Diagnostics, San Juan, Puerto Rico, USA). Serum cortisol was measured by RIA (Kit 1114; Immunotech International, Luminy-Marseille, France). Serum growth hormone and prolactin were measured by immunoradiometry (IRMA).

Acute-Phase Response. Serum interleukin 6 (IL-6) was measured by an enzymoimmunoassay technique with a microtiter plate (Medgenix, Fleurus, Belgium). The lower limit of detection of IL-6 activity is 5 pg/ml. C-reactive protein (CRP) was measured by nephelometry (Behring, Marburg, Germany), with a normal upper limit of 0.8 mg/dl. The prealbumin level was determined by nephelometric analysis.

Metabolic Response. Serum insulin was measured by RIA (INS-PR; Cis Bio International, F91192 Gif-Sur-Yvette, France). The glucagon level was determined by an RIA technique using the antibody 30K (Dr. R. Unger). Glucose was determined by an enzymatic measurement using the hexokinase method (autoanalyzer DAX). Lactate also was determined by enzymatic measurement, using the Bergmeyer technique (autoanalyzer RA-XT). Total proteins were assayed by the biuret method and albumin by the green bromocresol method in autoanalyzer DAX. Triglycerides were measured with the glycerol phosphate oxidase reaction (DAX 72), and free fatty acids were assayed enzymatically by the NEFA-PAP method (Lab. BioMerieux).

Laboratory Tests. Blood gases and pH were determined using the Corning gas analyzer. Red (RBC) and white (WBC) blood cell counts were done by automated analysis (Technicon H2).

Statistical Analysis. Statistical studies of the clinical results were performed with the standard χ^2 or Student *t*-test. Analysis of repeated measures was performed with the ANOVA test. To produce summary measures of the biochemical data [22] each parameter was plotted against time, and the area under the curve was calculated individually for each patient. Areas under the curve in the two groups were compared using the Student *t*-test.

Table 3. Patient characteristics.

Characteristic	Group I (CxL)	Group II (CxO)
No.	12	13
Age (years)	56 ± 13	61 ± 17
Sex (M/F)	5/7	3/10
ASA I/II	3/9	5/8
Previous abdominal surgery	3/12	5/13
Weight (kg)	68 ± 12	64 ± 14
Height (cm)	156 ± 20	160 ± 10

None of the differences between groups I and II were significant.

Table 4. Operative parameters.

Parameter	Group I (CxL)	Group II (CxO)	p
No.	12	13	
Anesthesia time (minutes)	100 ± 22	114 ± 41	NS
Intraoperative cholangiography (no.)	9/12	13/13	NS
Postoperative analgesia (doses)	2.7 ± 2.6	6.3 ± 4.6	0.03
Postoperative stay (days)	3.0 ± 0.7	5.6 ± 2.0	0.001

NS: not significant.

Results

Demographic features of the two groups are described in Table 3. The groups were well matched for age, sex, surgical risk, height, and weight. There were no differences in the anesthesia times. Intraoperative cholangiography was performed in 9 of 12 cases in group I and in all cases in group II (p = NS). No patient developed postoperative complications. Analgesia requirements ($p < 0.03$) and postoperative stay ($p < 0.001$) were significantly lower in group I (Table 4).

Cholecystectomy performed by either procedure induced a modification of the biochemical and hormonal parameters evaluated, with a significant increase over basal values for ACTH, cortisol, prolactin, glucose, lactate, IL-6, CRP, WBC count, and PCO_2 (ANOVA). Both models of surgical injury induced a significant reduction of prealbumin, total proteins, albumin, free fatty acids, hemoglobin, hematocrit, and pH. There were no differences between the values of growth hormone, insulin, glucagon, or PO_2 during any of the periods studied. The trygliceride levels, however, were significantly modified only in group I.

Comparison of the results for the two operative techniques (area under the curve) reveals that in group I (CxL) there was significantly less increase in the values of the positive acute-phase response markers IL-6 (17 ± 17 versus 47 ± 26 pg/ml × hr × 10^2; $p < 0.003$), CRP (16 ± 12 versus 35 ± 16 mg/dl × hr × 10; $p < 0.004$); and there was less decrease in prealbumin (16.0 ± 2.7 versus 13.8 ± 2.3 mg/dl × hr × 10^2; $p < 0.05$), a negative acute-phase response marker (Table 5, Figs. 1–3).

Discussion

Laparoscopic cholecystectomy has become the standard treatment for gallstones. Several studies have demonstrated the superiority of the laparoscopic technique over the open technique, as it is followed by a shorter postoperative stay and a more rapid return to normal activity [1–3].

Table 5. Biochemical responses.

	CxL[a]	CxO[a]	p[b]
Neuroendocrine response			
ACTH (pg/ml × hr × 10^2)	36 ± 46	39 ± 20	NS
Cortisol (μg/ml × hr × 10^{-2})	14 ± 2	17 ± 3	NS
Growth hormone (ng/ml × hr × 10)	15 ± 14	36 ± 49	NS
Prolactin (ng/ml × hr × 10^2)	15 ± 12	13 ± 6	NS
Acute-phase response			
Interleukin 6 (pg/ml × hr × 10^2)	17 ± 17	47 ± 26	0.001
C-reactive protein (mg/dl × hr × 10)	16 ± 12	35 ± 16	0.005
Prealbumin (mg/dl × hr × 10^2)	16 ± 2	13 ± 2	0.05
Metabolic response			
Insulin (mU/L × hr × 10^2)	17 ± 17	12 ± 7	NS
Glucagon (pg/ml × hr × 10^2)	71 ± 30	91 ± 27	NS
Glucose (mg/dl × hr × 10^2)	88 ± 14	101 ± 20	NS
Lactate (mg/dl × hr × 10)	73 ± 22	82 ± 22	NS
Total proteins (g/L × hr × 10^2)	45 ± 2	44 ± 7	NS
Albumin (g/L × hr × 10^2)	26 ± 1	26 ± 1	NS
Triglycerides (mg/dl × hr × 10^2)	81 ± 31	75 ± 19	NS
Free fatty acids (μmol/L × hr × 10^3)	55 ± 23	49 ± 17	NS
Blood gases and pH			
pH (× hr × 10)	53.0 ± 0.3	56.0 ± 2.0	NS
PO_2 (mm Hg × hr × 10^2)	59.0 ± 42.0	59.0 ± 82.0	NS
PCO_2 (mm Hg × hr × 10^2)	26.0 ± 2.0	25.0 ± 1.5	NS
Hematologic parameters			
Hematocrit (L/L × hr × 10^2)	26.0 ± 2.7	26.0 ± 3.2	NS
Hemoglobin (g/L × hr × 10^2)	8.8 ± 1.0	8.9 ± 0.9	NS
Leukocyte count (× 10^9/L × hr × 10)	50.0 ± 9.0	60.0 ± 14.0	NS

[a]Changes expressed as area under the curve.
[b]Student's t-test.

The observation of these satisfactory results has prompted analysis and investigation of the factors that may account for the rapid recovery after the laparoscopic technique in contrast with the open procedure. It may be due to the lesser surgical trauma involved. Several studies have compared the injury response to the two techniques, but the results are contradictory and there is no consensus [8–20].

This study confirms that cholecystectomy, performed by open or laparoscopic technique, induces significant surgical injury, as

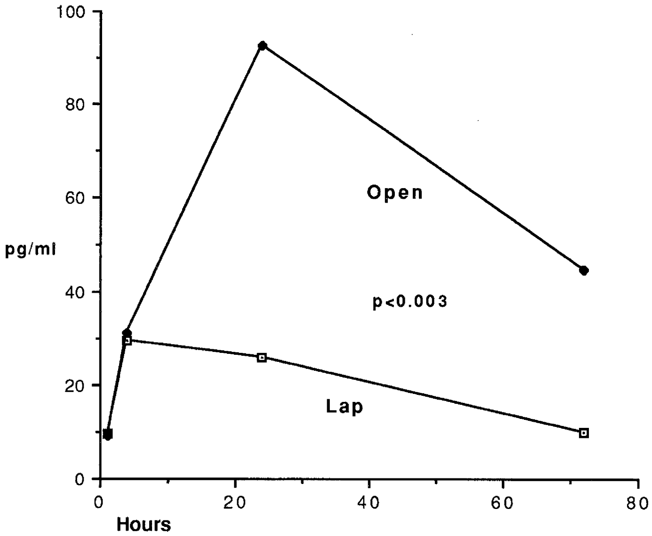

Fig. 1. Interleukin 6 levels after open cholecystectomy were significantly higher than after laparoscopic cholecystectomy ($p < 0.003$, area under the curve).

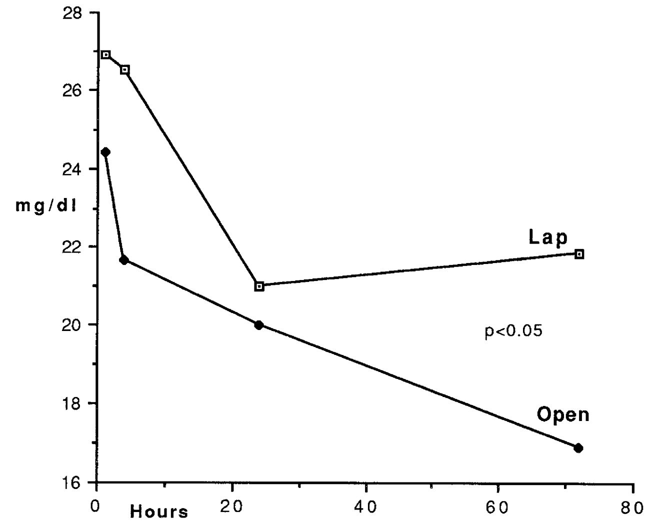

Fig. 3. Laparoscopic cholecystectomy induces a smaller decrease in prealbumin than open cholecystectomy ($p < 0.05$, area under the curve).

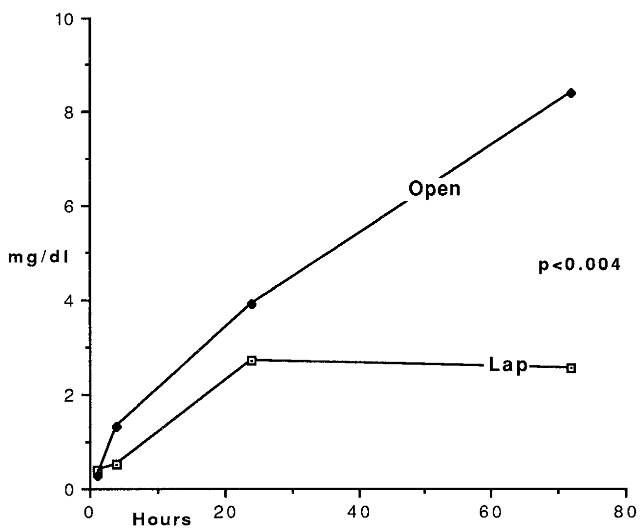

Fig. 2. Open cholecystectomy induces a higher increment in C-reactive protein than laparoscopic cholecystectomy ($p < 0.004$, area under the curve).

demonstrated by a substantial rise in the parameters measured, but this response was qualitatively different in the two groups. The rise in IL-6 and CRP levels (positive markers) and the fall in prealbumin (negative marker) were less marked in the laparoscopic group, suggesting that the acute-phase response was less intense.

A component of the response to surgical injury is the neuroendocrine stimulation of the hypothalamus–hypophyseal–adrenal axis, with an increase in the release of ACTH, cortisol, and catecholamines [5]. We observed a greater rise of ACTH and cortisol in group II than in group I, although the difference was not significant. We found no differences in insulin, glucagon, growth hormone, or prolactin. MacMahon et al. [12], Joris et al. [13], and Jakeways et al. [10] found no differences in the values of cortisol or catecholamines between the groups. However, Papalois et al. [14] and Dionigi et al. [19] reported a rise in cortisol in the open-surgery group. These results differ from those of Dietrich et al. [11], who observed an increase in ACTH, cortisol, prolactin, and growth hormone in the laparoscopic group and concluded that laparoscopy is a stress factor.

Although there is no general agreement, analysis of the results suggests that the laparoscopic surgical model induces neuroendocrine stimulation similar to that of the open surgical model, with a lower increase in ACTH and cortisol and a minimal influence on the rest of hypophysical (growth hormone, prolactin) and counterregulatory (insulin and glucagon) hormones.

An important component of the global biologic response to injury is the acute-phase response. After tissue trauma or infection, a complex series of reactions are executed by the host in an effort to prevent ongoing tissue damage, isolate and destroy the infective organism, and activate the repair processes that are necessary to return the organism to normal function. The early and immediate set of reactions that are induced are collectively known as the acute-phase response [23, 24]. This response begins in the wound site with the activation of leukocytes, fibroblasts, and endothelial cells and the release of cytokines. Research into a number of cytokines has identified the key role of tumor necrosis factor alpha (TNFα) and IL-6 as local mediators [25–30] and as responsible for this acute-phase response [23, 24]. These local mediators induce a systemic reaction characterized by fever, leukocytosis, activation of complement, a negative nitrogen balance, and important changes in the concentration of some plasma proteins. IL-6 induces the synthesis of specific hepatic proteins (acute-phase proteins), the most important of which is CRP (positive marker), which shows a rapid, marked, specific increase after trauma [24]. Furthermore, there is a relation between the acute phase and the neuroendocrine response, with a stimulating effect induced by IL-6 [28]. It has been shown that IL-6 and CRP correlate with the degree and amount of surgical injury (wound "volume"), blood loss, and duration of the surgical procedure; and they can be used as parameters for measuring the amount of tissue damage [25–31].

The observation of significantly higher values of IL-6 and CRP in the laparoscopy group suggests that the acute-phase response after open surgery is more intense than after laparoscopic cholecystectomy, which in turn indicates less surgical injury during laparoscopic cholecystectomy. In this study, blood loss was similar, with no modification of hematocrit or hemoglobin in either group; and the duration of the anesthesia was similar. The differential factor between the surgical procedures was the "wound volume," comparing the standard 8- to 10-cm subcostal incision in the open group with the four punctures used for the laparoscopic approach.

Eight studies have analyzed modification of the CRP [9, 11–13, 15, 18–20], and six have analyzed the IL-6 changes [12, 13, 16–18, 20] (Table 1). Six report that the acute-phase response is less intense after laparoscopic surgery than after open surgery, in agreement with the results in our study. MacMahon et al. [12] and Berggren et al. [18], in a prospective and randomized study comparing laparoscopic cholecystectomy with minicholecystectomy, found no significant differences between the groups after studying IL-6 and CRP levels. Both studies suggest that the wide interindividual differences and the fact that most studies were not randomized introduced a possible bias in favor of the laparoscopy groups. McMahon et al. [12] compared laparoscopic cholecystectomy with minicholecystectomy, a surgical procedure in which a short incision is used. Berggren et al. [18], in a study with results similar to those of McMahon et al. [12], measured IL-6 and CRP levels 24 hours after surgery (the patients were discharged early). Vander Velpen et al. [17] found no difference after measuring the IL-6 response with a biologic assay. In our study laparoscopic cholecystectomy was compared with cholecystectomy using a standard 8- to 10-cm subcostal incision; values were recorded for 3 days, allowing us to detect the modifications of IL-6, which begin to rise between 1 and 24 hours, and CRP, which began to increase 24 hours after the surgical injury. On the other hand, the response was quantified by calculating the area under the curve, a statistical method that permits better understanding of biologic changes due the wide interindividual differences.

These differences are probably due to the avoidance of the laparotomy wound [9] and to the lesser intraabdominal tissue damage secondary to intraoperative manipulation or desiccation of exposed tissues. The parietal "wound volume" is the main difference between the two surgical models of injury and may explain the better clinical results also obtained after minicholecystectomy. Bowel manipulation and desiccation, other components of the "operative wound" during surgery, fare better during laparoscopy. Shimada et al. [32] showed that bowel manipulation induced a rise in IL-6, and Grablowitz et al. [33] recovered fewer mesothelial peritoneal cells—used as markers of tissue damage—after postoperative intraabdominal lavage in patients operated by laparoscopy than in open cases.

The surgical injury response after laparoscopic cholecystectomy is similar to that following open surgery, but the acute-phase response component is significantly less intense. This finding may be a consequence of the reduction in the volume of the operative wound during laparoscopic cholecystectomy.

Résumé

La démonstration objective d'une meilleure récupération clinique postopératoire suggère que la réponse à l'agression induite par la chirurgie sous coelioscopie est moins importante qu'après la chirurgie ouverte. On a étudié de façon prospective 25 patients ayant une lithiase vésiculaire non compliquée. Les patients ont été opérés soit par coelioscopie (groupe I, CC; n = 12) soit par laparotomie (groupe II, CO: n = 13). Les besoins en analgésie ($p < 0.026$) et la durée de séjour ($p < 0.001$) ont été significativement moins importants dans le groupe I (CC). Quel que soit le type de cholécystectomie, les valeurs de base du glucose, des lactates, des globules blancs, de la prolactine, de l'ACTH, du cortisol, de l'interleukine 6, de la C-réactive protéine et de la PCO2 étaient élevées de façon significative. Les deux méthodes ont été responsables d'une réduction significative des protéines totales, de l'albumine, de la préalbumine, des acides gras libres, de l'hémoglobine, de l'hématocrite et des valeurs du pH. Il n'y avait, par contre, aucune différence dans les valeurs de l'hormone de croissance, de l'insuline, du glucagon ou de la PO2, quelle que soit la période étudiée. La comparaison des deux techniques de cholécystectomie a montré que la cholécystectomie sous coelioscopie induisait une phase aiguë significativement moins intense (aire sous la courbe) en ce que concerne l'interleukine 6 (17 ± 17 vs 47 ± 26 pg/ml $\times$ h $\times 10^2$; $p < 0.003$), la C-réactive protéine (16 ± 12 vs 35 ± 16 mg/dl $\times$ h $\times$ 10; $p < 0.004$) et la préalbumine (16 ± 2.7 vs 13.8 ± 2.3 mg/dl $\times$ h $\times 10^2$; $p < 0.05$). La réponse à l'agression après cholécystectomie par coelioscopie est similaire à la cholécystectomie ouverte, mais la réponse de la phase aiguë est moins intense. Ces données sont peut-être la conséquence de la réduction de l'importance de la plaie opératoire lors de la cholécystectomie par coelioscopie.

Resumen

La demostración objetiva de una mejor recuperación postoperatoria sugiere que la respuesta al trauma quirúrgico que induce el abordaje laparoscópico es menos intenso que la de la cirugía abierta. Veinticinco pacientes diagnosticados como colelitiasis no complicada, fueron estudiados en forma prospectiva: intervenidos por laparoscopia (Grupo I, CxL, N:12) o por cirugía abierta (Grupo II, CxA, N:13). Los requerimientos de anestesia ($p < 0.026$) y estancia postoperatoria ($p < 0.001$) fueron significativamente menores en el Grupo I (CxL). La colecistectomía practicada mediante las dos opciones técnicas indujo un aumento significativo sobre los valores basales de glucosa, lactato, recuento de leucocitos, prolactina, ACTH, cortisol, interleucina-6, proteína C reactiva y PCO2. Ambos tipos de procedimiento quirúrgico indujeron una reducción significativa de la proteínas totales, albúmina, prealbúmina, ácidos grasos libres, hemoglobina, hematocrito y pH. No se hallaron diferencias en los valores de hormona de crecimiento, insulina, glucagón o PO2, en ninguno de los períodos estudiados. La comparación de los resultados de las dos técnicas de colecistectomía demostró que la colecistectomía laparoscópica indujo una respuesta de fase aguda significativamente menos intensa (área por debajo de la curva) de interleucina-6 (17 ± 17 vs 47 ± 26 pg/ml $\times$ h $\times$ 102, $p < 0.003$), proteína C reactiva (16 ± 12 vs 35 ± 16 mg/dl $\times$ h $\times$ 102, $p < 0.004$) y prealbúmina (16 ± 2.7 vs 13.8 ± 2.3 mg/dl $\times$ h $\times$ 102, $p < 0.05$). La respuesta al trauma quirúrgico después de la colecistectomía laparoscópica

es similar a la de la colecistectomía abierta, pero el componente de respuesta de fase aguda es menos intenso. Este hallazgo puede significar que ello se debe a la reducción de la magnitud de la herida quirúrgica en la colecistectomía laparoscópica.

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Invited Commentary

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This study compares patients' responses to open versus laparoscopic cholecystectomy with regard to clinical outcome (consumption of analgesics and hospital stay) and biochemical trauma indicators, including acute-phase reactants, neuroendocrine hormones, and metabolic parameters, as well as such standard variables as acid-base balance and hematology. The principal findings are significantly larger aberrations in acute-phase reactants after laparotomy.

The most striking negative character of this study is the determination to analyze these previously investigated parameters in patients undergoing cholecystectomy for uncomplicated cholelithiasis without application of a randomized selection strategy. Other attempts in this regard have supported striking interindividual alterations with respect to essentially all the currently explored variables, and this circumstance has been considered to substantially influence the outcome of statistical comparisons [1, 2]. Although the authors of the present material fail to demonstrate differences of statistical significance between the limited number of patients in each subgroup, Table 3 of the paper suggests discrepancies of potential significance mainly with respect to the distribution of gender and ASA classes [3]. Because no data are provided as to the criteria for selecting patients into each operative group the results must be interpreted with caution.

Disregarding these limitations, the authors substantiate less severe acute-phase responses to the laparoscopic approach, whereas a host of other parameters shift to variably similar extents in the two patient subgroups. In comparison to a previous investigation utilizing the same IL-6 assay [2], the currently attained difference of statistical significance seems mainly to relate to substantially higher IL-6 levels 24 hours after laparotomy (about 92 pg/ml versus 61 mg/L). This difference was further augmented by the present observation of lower IL-6 levels in the laparoscopy group in comparison to the previous study. The cause of these discrepancies is unclear but seems unrelated to the length of the subcostal incision or the duration of anesthesia, at least in the group subjected to open cholecystectomy. It is noteworthy, however, that the present study encompasses only single estimates of IL-6 at each investigated point of time. Our experience favors invariable use of duplicate estimations due to intraassay variations.

Nevertheless it is striking that the differences in biochemical responses to open versus laparoscopic cholecystectomy essentially are limited to acute-phase reactions, although some previous studies have substantiated that the open approach is accompanied by greater cortisol, catecholamine, glucose, and leukocyte responses (for references see Table 1 of Targarona et al.). Moreover, there is contrasting evidence suggesting that laparoscopy is accompanied by enhanced cortisol, catecholamine, and ACTH responses [4, 5]. Because the clinical responses to uncomplicated laparoscopic cholecystectomy generally are strikingly favorable in comparison at least to conventional laparotomy, it may be argued that the biochemical responses studied in this and previous studies are somewhat irrelevant and we should search for more clinically relevant variables to study.

This clinically favorable outcome of the laparoscopic operation generally is consistent with the observations on requirements of injectable analgesics and duration of hospitalization. Also in these respects, the study is essentially confirmative, as especially the hospital stay has been examined in a considerably larger series of patients randomized to open and laparoscopic cholecystectomy [3, 6].

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