Changes in Breathing Control and Mechanics After Laparoscopic vs Open Cholecystectomy

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Hypothesis: We hypothesized that there might be different effects on breathing control and respiratory mechanics after laparoscopic vs open cholecystectomy.

Design: Randomized clinical trial.

Setting: A general hospital in Greece.

Patients: Of 53 patients assessed for eligibility, 18 and 10 were randomly allocated to the laparoscopic and open cholecystectomy groups, respectively. These 28 patients had normal spirometry measurements and American Society of Anesthesiologists' class I physical status.

Main Outcome Measures: Measurements of breathing control and mechanics variables. Tidal volume, inspiratory time, breathing frequency, mean inspiratory flow, duty cycle, central respiratory drive, and mean inspiratory impedance were recorded before surgery on the second and eighth postoperative days. Airway resistance was recorded before surgery and on the eighth postoperative day, with all measurements being performed under no influence of analgesia.

Results: Two days after surgery, inspiratory time, breathing frequency, and central respiratory drive were significantly changed compared with preoperative values for both methods, whereas mean inspiratory impedance was significantly increased ($P<.001$) for the laparoscopic procedure. Eight days after surgery, changes were seen only for the laparoscopic group: duty cycle and airway resistance were significantly reduced ($P=.01$) and increased ($P=.04$), respectively, compared with preoperative data.

Conclusion: Laparoscopic cholecystectomy seems to be associated with small but sustained alterations in the control of breathing and mechanics, which might have an unfavorable clinical impact on patients with compromised lung function.

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PREVIOUS STUDIES[1-4] HAVE shown the impact of upper abdominal operations on the control of breathing and lung mechanics variables in the early postoperative period. Particularly, the effect of gallbladder removal on breathing patterns[1-3] and airway resistance (Raw)[4] has been studied immediately after laparoscopic cholecystectomy (LC),[1] on the first day after LC and open cholecystectomy (OC),[2,3] on the third day after OC,[2] and 2 days after LC and OC.[4]

Breathing frequency (BF), inspiratory time (T_i) and expiratory time, tidal volume (V_T), and mean inspiratory flow rate (V_T/T_i), were found to be altered as a result of gallbladder removal, as is evident from data for the first[2,3] and third[2] postoperative days after LC and OC.[2,3] Duty cycle (T_i/T_{TOT})[1,3] and mean inspiratory flow[1] were studied 3 hours[1] and 24 hours[3] after LC; there was a significant reduction in T_i/T_{TOT} in the very early postoperative period.[1]

Central respiratory drive (as expressed by $P_{0.1}$) and mean inspiratory impedance ($Z_{m,insp}$) (represented by the ratio $P_{0.1}/[V_T/T_i]$)[5,6] were also examined 3 hours after LC without detection of statistically significant changes.[1] Another study[7] found that respiratory system impedance was considerably increased after the introduction of pneumoperitoneum during LC and that it remained elevated even after carbon dioxide (CO_2) release from the abdomen. Several other studies have shown that regardless of the surgical method used for cholecystectomy (laparoscopic or open), there is a reduction in overall abdominal compartment movement[2,3] and in diaphragmatic activity.[1,8-11]

To our knowledge, there have been no studies of OC and LC examining possible changes in the aforementioned variables on a longer-term basis. Such studies could provide a helpful means of assessing respiratory performance at a later time after surgery. The aim of the present study is to investigate any sustained impact of either type of surgery on control of breathing and lung mechanics variables extending to the eighth postoperative day. By that time, patients are expected to have been discharged from the hospital and to have returned to their usual daily activities. Longer follow-up would offer useful clinical information regarding the comparative longer-term effects of either surgical method.

METHODS

PATIENTS

The inclusion criteria were approved by the Department of Experimental Physiology, Faculty of Medicine, Athens University (which authorized the performance of the investigation), and the Research Ethics Committee of the Red Cross General Hospital of Athens (one of the biggest general hospitals in Athens), from which patients were recruited. Patients should (1) have symptomatic cholecystolithiasis without cystic or common bile duct gallstones, (2) be 68 years or younger (range, 30-68 years), (3) be free of any signs or symptoms of active or concurrent disease except for the gallbladder problem, (4) have no regular use of any type of medication, (5) have normal spirometry measurements, (6) have an American Society of Anesthesiologists' class I physical status, (7) not be morbidly obese (body mass index [calculated as weight in kilograms divided by the square of height in meters] <40),[12] and (8) have had no previous thoracic or abdominal operations. Written informed consent was obtained from all the patients before participation in this institutionally approved study protocol.

Preoperative examinations included history, physical examination, full blood and biochemistry tests, chest radiographs, spirometry, electrocardiography, echocardiography, and upper abdominal ultrasonography. All these examinations were performed in the last 3 days before surgery. Our intention was to conduct a study of surgical research recording the effect of gallbladder removal performed using either LC or OC for symptomatic cholecystolithiasis on the control of breathing and respiratory mechanics variables.

Patients arriving at the emergency department for symptomatic cholecystolithiasis were registered by the surgical resident on call. The day after hospital admission, patients were randomly allocated (no blocking and no stratification) by the attending physician (who was the same during the entire allocation period) to the LC or OC group. The random allocation was generated by separating patients into triads according to their registration sequence at the emergency department. The first patient of each triad was scheduled for OC and the second and third patients for LC. The random allocation sequence was concealed until interventions were assigned.

Fifty-three patients were assessed for eligibility. Enrollment of participants in the study was performed by one of us (G.D.B.) according to the inclusion criteria. Eleven patients were disqualified because they did not meet the inclusion criteria, 7 refused to participate, and 3 were excluded for other specific reasons (recent use of illicit drugs [n=1] and inability to perform the maneuvers required for the measurements at initial screening [n=2]). The remaining 32 patients were assigned by one of us (G.D.B.) to surgical groups performing LC (n=19) and OC (n=13) (**Figure 1**).

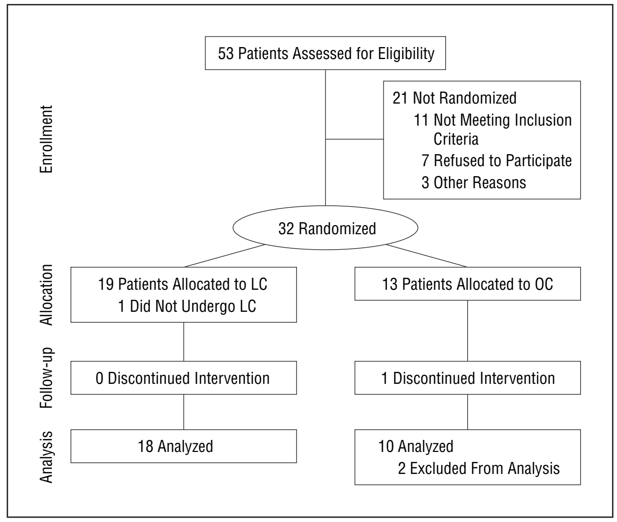

Figure 1. Flow diagram of the patients through the phases of the randomized trial. LC indicates laparascopic cholecystectomy; OC, open cholecystectomy.

STUDY DESIGN

For both surgical procedures, control of breathing indexes were measured before surgery and on the second and eighth postoperative days. Control of breathing indices included V_T (in liters), T_i (in seconds), BF (in breaths per minute), mean V_T/T_i (in liters per second), T_i/T_{TOT}, mouth pressure generated 100 milliseconds after the onset of an occluded inspiration ($P_{0.1}$) (in centimeters of water), and $Z_{m,insp}$ ($P_{0.1}/[V_T/T_i]$) (in centimeters of water per liter per second).[5,6] Airway resistance (in centimeters of water · liters^{-1} · seconds) was examined for all the patients before surgery and on the eighth postoperative day.

MEASUREMENTS

All preoperative and postoperative measurements for control of breathing and airways resistance indices were performed in the Pulmonary Function Laboratory of the Intensive Care Unit of the Red Cross General Hospital of Athens by 1 of us (G.D.B.) using a cardiopulmonary gas exchange system (CPX/MAX; MedGraphics, St Paul, Minn) and a body plethysmography system (model 1085D; MedGraphics), respectively. The physician who performed the measurements was masked regarding the type of operation that each patient would undergo or had already undergone. The success of the masking was established by the fact that (1) the measurements were performed in a separate lung function department not related to the surgical unit, (2) each patient's medical records were not sent to the laboratory during measurements, and (3) 1 of us (G.D.B.) accompanied every patient during the measurements to ensure that no information was transferred from the patient to the lung function physician.

All the patients underwent testing in the seated position according to American Thoracic Society guidelines,[13] and they were not receiving any kind of respiratory or other medication therapy that could affect respiratory function before surgery or during the study. Data for measured variables were stored in the computer for future masked analysis as to whether the patient had OC or LC.

For each of the control of breathing indices, 20 respiratory cycles were registered, the first 4 of which were rejected because they represented the patient's period of adaptation to the equipment. During Raw testing, the best of 3 attempts was recorded for further analysis. Four hours after surgery, all the patients were given 2 glycerol suppositories for stool provocation, each containing 2.4 g of glycerol, 0.6 g of gelatin, and 0.3 g of demineralized water. On administration of the glycerol suppositories, auscultation of the abdomen was repeated every 2 hours until restitution of intestinal peristalsis. Normal

Table 1. F Values for the Control of Breathing Variables Measured Using 1-Way Analysis of Variance: Preoperative and Second and Eighth Postoperative Day Values

Variable	Laparoscopic Cholecystectomy Group (n = 18)*	Open Cholecystectomy Group (n = 10)†
V_T	1.24	2.6
T_i	13.828‡	3.939§
BF	12.277‡	7.198‖
V_T/T_i	2.252	0.210
T_i/T_{TOT}	7.77¶	6.75#
$P_{0.1}$	15.54‡	6.737#
$Z_{m,insp}$	9.463‡	2.109

Abbreviations: BF, breathing frequency; $P_{0.1}$, central respiratory drive; T_i, inspiratory time; T_i/T_{TOT}, duty cycle; V_T, tidal volume; V_T/T_i, inspiratory flow rate; $Z_{m,insp}$, mean inspiratory impedance.
*Data are given as $F_{2,34}$.
†Data are given as $F_{2,18}$.
‡$P<.001$.
§$P=.04$.
‖$P=.005$.
¶$P=.002$.
#$P=.007$.

peristalsis was restored 13 to 21 hours after LC and 20 to 37 hours after OC. The mean hospital stay after surgery was 2 days for the LC group and 6 days for the OC group.

ANESTHESIA AND THE SURGICAL PROCEDURE

All the participants underwent surgery between 8 AM and noon. The same anesthetic protocol was used for both surgical methods. Sixty minutes before surgery, 150 mg of ranitidine hydrochloride was given orally, and meperidine hydrochloride (0.5 mg/kg) plus cefamandole nafate (1 g/vial ×2) were administered intramuscularly. A urinary bladder catheter and a nasogastric tube were placed in all the patients before surgery. General anesthesia was induced with the intravenous administration of fentanyl citrate (2 μg/kg), propofol (2 mg/kg), and atracurium besylate (0.5 mg/kg). After tracheal intubation, anesthesia was maintained using a mixture of 4 liters of oxygen, 4 liters of nitrogen hypoxide, and 1% desflurane at an end-tidal concentration of 6.1% (1 minimum alveolar concentration). In addition, atracurium (0.3 mg/kg) was intravenously injected once every hour. Fentanyl was intravenously administered once just before surgical incision at a dose of 5 μg/kg and every 30 minutes during the procedure at a dose of 2 μg/kg. Controlled ventilation was administered using volume-cycled ventilators (Engström EAS 9010, Gambro Engström AB, Bromma, Sweden), with a frequency of 12 to 14 breaths/min. Before CO_2 insufflation into the abdominal cavity, the lungs were ventilated using a V_T of 8 to 10 mL/kg to keep end-tidal P_{CO_2} levels between 30 and 40 mm Hg. Throughout anesthesia, a monitor (Cardiocap, Datex-Ohmeda Inc, Madison, Wis) was used to provide continuous information on electrocardiography, blood pressure, partial pressure of end-tidal CO_2, and oxygen-hemoglobin saturation. Ten minutes before the end of the operation, desflurane and atracurium administration were simultaneously interrupted. As soon as even minimal muscular function recovery was evident, the residual neuromuscular blockade was reversed using neostigmine methylsulfate (0.5 mg/kg) plus atropine sulfate (0.02 mg/kg) in the same syringe. For the LC group, the surgical procedure was performed using a standard 4-trocar technique with the surgeon standing to the left of the patient, and pneumoperitoneum was established and maintained by insufflation of CO_2 to a pressure of approximately 12 to 13 mm Hg using insufflation equipment (model UHI-2; Olympus, Tokyo, Japan). For the OC group, surgery was performed in the standard manner through a 15-cm right oblique subcostal incision (Kocher incision). The duration of surgery was 80 to 100 minutes for the OC group and 60 to 80 minutes for the LC group.

PAIN ASSESSMENT

No analgesics were used before surgery. Postoperative analgesia was intramuscularly administered over the deltoid muscle using meperidine hydrochloride (25 mg) within approximately 8 hours after surgery in the LC and OC groups. The same dose was required 12 hours after the first administration in all the OC patients and in 2 patients in the LC group. Particularly, for patients undergoing OC, 200 mg of ropivacaine diluted in 20 mL of isotonic sodium chloride was intramuscularly administered to abdominal muscles before wound closure for the management of acute pain. Infiltration anesthesia and a field block of ropivacaine,[14-16] resulting in facilitation of the respiration by reducing pain from the abdominal trauma, is considered critical to prevent atelectasis in the early postsurgical period.

STATISTICAL ANALYSIS

Data were normally distributed. Comparisons of baseline values between the 2 groups were performed using the *t* test or the Welch test (in cases of unequal variances). No statistically significant differences were found regarding baseline (preoperative) values between the 2 groups. Changes across time for each group (baseline values vs the second and eighth postoperative day values) were determined using 1-factor repeated-measures analysis of variance, and statistically significant differences were evaluated using the F distribution values (**Table 1**). Then, a pairwise multiple comparisons procedure (Tukey critical difference) was performed.

Differences across time between LC and OC were evaluated after having calculated for all studied variables' mean percentage changes and 95% confidence intervals (CIs) from baseline to the second and eighth postoperative days. The mean percentage changes for each variable in either group were determined by estimating the percentage change in each patient separately from baseline to the second and eighth postoperative days and then estimating the mean for the second and eighth postoperative days for each group. Comparisons between the 2 groups were made using the *t* test or the Welch test as appropriate. All tests were 2-sided, the level of significance having been set at $P=.05$. All the analyses were performed using a statistical software program (SPSS for Windows, version 8.00; SPSS Inc, Chicago, Ill).[17]

RESULTS

Of 19 patients randomly assigned to the LC group, 1 did not receive the allocated intervention because he left the hospital before undergoing surgery. Of 13 patients randomly assigned to the OC group, 1 did not undergo postoperative measurements owing to equipment failure and 2 were excluded from the analysis stage because of complications attributed to the surgical procedure (placing a Kehr tube because of a small gallstone sliding into the common bile duct during surgical manipulations for

Table 2. Measured Variables and Percentage Changes for the Laparoscopic and Open Cholecystectomy Groups

Variable	Preoperative Value, Mean ± SD	Second Postoperative Day Value, Mean ± SD	Change From Preoperative to Second Postoperative Day, Mean ± SEM (95% CI), %	Eighth Postoperative Day Value, Mean ± SD	Change From Preoperative to Eighth Postoperative Day, Mean ± SEM (95% CI) %
Laparoscopic Cholecystectomy Group					
V_T, L	0.52 ± 0.17	0.48 ± 0.13	−4.11 ± 3.48 (−5.84 to −2.38)	0.49 ± 0.15	−2.41 ± 5.24 (−5.01 to 0.19)
T_i, s	1.26 ± 0.27	1.13 ± 0.24*	−10.18 ± 1.74 (−11.04 to −9.32)	1.23 ± 0.30	−2.13 ± 1.71 (−2.98 to −1.28)
BF, bpm	20.57 ± 5.80	22.58 ± 4.90†	11.79 ± 3.37 (10.12 to 13.46)	19.62 ± 4.52	−3.34 ± 2.78 (−4.72 to −1.96)
V_T/T_i, L/s	0.56 ± 0.33	0.47 ± 0.13	−4.04 ± 6.17 (−7.11 to −0.97)	0.46 ± 0.17	−8.67 ± 6.60 (−11.95 to −5.39)
T_i/T_{TOT}	0.41 ± 0.05	0.40 ± 0.04	−0.57 ± 1.93 (−1.53 to 0.39)	0.38 ± 0.04†	−6.08 ± 2.29 (−7.22 to −4.94)
$P_{0.1}$, cm H_2O	1.64 ± 0.39	2.09 ± 0.61‡	29.88 ± 8.47 (25.67 to 34.09)	1.59 ± 0.44	−1.92 ± 5.35 (−4.58 to −0.74)
$Z_{m,insp}$, cm $H_2O \cdot L^{-1} \cdot s^{-1}$	3.51 ± 1.35	4.62 ± 1.45*	50.74 ± 19.66 (40.96 to 60.51)	3.74 ± 1.24	21.18 ± 14.06 (14.19 to 28.17)
Raw, cm $H_2O \cdot L^{-1} \cdot s$	1.59 ± 0.36 (85.29 ± 20.90‖)	NA	NA	1.86 ± 0.65§ (101.39 ± 34.17‖)	16.64 ± 7.44 (12.94 to 20.34)
Open Cholecystectomy Group					
V_T, L	0.55 ± 0.11	0.54 ± 0.12	1.73 ± 8.49 (−7.84 to 4.38)	0.52 ± 0.05	−3.46 ± 3.94 (−6.3 to −0.62)
T_i, s	1.24 ± 0.29	1.11 ± 0.17¶	−8.46 ± 5.62 (−12.51 to −4.41)	1.26 ± 0.16	4.22 ± 5.20 (0.48 to 7.96)
BF, bpm	20.86 ± 5.96	25.44 ± 6.62¶	25.83 ± 8.61 (19.63 to 32.03)	19.45 ± 3.64	−4.25 ± 4.15 (−7.24 to −1.26)
V_T/T_i, L/s	0.65 ± 0.53	0.66 ± 0.54	2.95 ± 7.97 (−2.79 to 8.69)	0.64 ± 0.56	−4.55 ± 3.55 (−7.11 to −1.99)
T_i/T_{TOT}	0.40 ± 0.04	0.43 ± 0.03	7.93 ± 3.17 (5.65 to 10.21)	0.40 ± 0.04	−0.69 ± 2.25 (−2.31 to 0.93)
$P_{0.1}$, cm H_2O	1.55 ± 0.17	1.91 ± 0.36#	24.20 ± 7.74 (18.63 to 29.77)	1.52 ± 0.26	−1.10 ± 6.04 (−5.49 to 3.25)
$Z_{m,insp}$, cm $H_2O \cdot L^{-1} \cdot s^{-1}$	3.04 ± 1.03	3.65 ± 1.19	25.02 ± 9.62 (18.35 to 31.69)	3.21 ± 1.38	5.16 ± 7.69 (−0.38 to 10.7)
Raw, cm $H_2O \cdot L^{-1} \cdot s$	1.93 ± 1.10 (119.78 ± 65.25‖)	NA	NA	1.94 ± 0.67 (123.33 ± 45.87‖)	18.06 ± 14.73 (7.45 to 28.67)

Abbreviations: BF, breathing frequency; CI, confidence interval; NA, not assessed; $P_{0.1}$, central respiratory drive; Raw, airway resistance; T_i, inspiratory time; T_i/T_{TOT}, duty cycle; V_T, tidal volume; V_T/T_i, inspiratory flow rate; $Z_{m,insp}$, mean inspiratory impedance.

*$P<.001$.

†$P=.01$.

‡$P=.001$, second postoperative day vs preoperative.

§$P=.04$, comparison between eighth postoperative day and preoperative.

‖Percent predicted.

¶$P=.05$.

#$P=.01$, second postoperative day vs preoperative.

1 patient and a febrile episode 30 hours after surgery associated with inflammation at the surgical incision site for the other).

This study was conducted for 12 months (with full analysis of the studied patients completed in September 2002). The 18 patients in the LC group (13 women and 5 men) and the 10 patients in the OC group (7 women and 3 men) included in the analysis stage were homogeneous, and there was no statistically significant difference between them regarding mean±SD age (LC group: 52.56±12.16 years; OC group: 54.80±9.21 years; $P=.68$) and mean±SD body mass index (LC group: 27.60±3.5; OC group: 27.90±2.7; $P=.84$).

Nine of the 28 participants (5 in the LC group and 4 in the OC group) smoked fewer than 10 cigarettes per day. The remaining 19 patients were nonsmokers. Preoperative measurements for spirometry (forced vital capacity, forced expiratory volume in 1 second, and forced expiratory volume in 1 second–forced vital capacity ratio), maximal midexpiratory flow rate (forced expiratory flow between 25% and 75%), and inspiratory capacity were normal for all analyzed patients, and there was no statistically significant difference between the 2 groups regarding the aforementioned variables expressed as a percentage of their predicted normal values.

Control of breathing and Raw measurements for the LC and OC groups are given in **Table 2**. Statistically documented differences are as follows:

On the second postoperative day there was a significant reduction in T_i (LC group: $P<.001$; 95% CI, 1.01-1.25; OC group: $P=.05$; 95% CI, 0.99-1.23) and a sig-

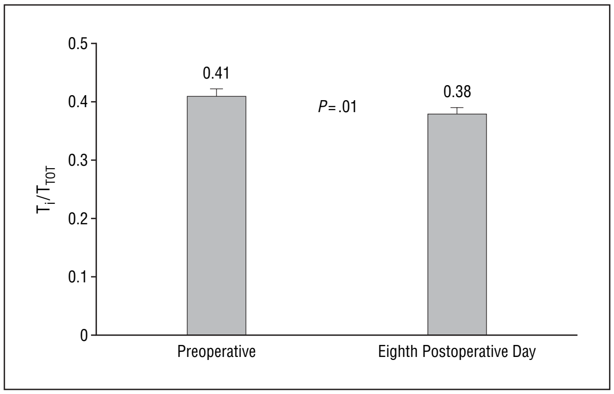

Figure 2. Mean preoperative and eighth postoperative day duty cycle (T_i/T_{TOT}) values in the laparoscopic cholecystectomy group. Error bars represent SEM.

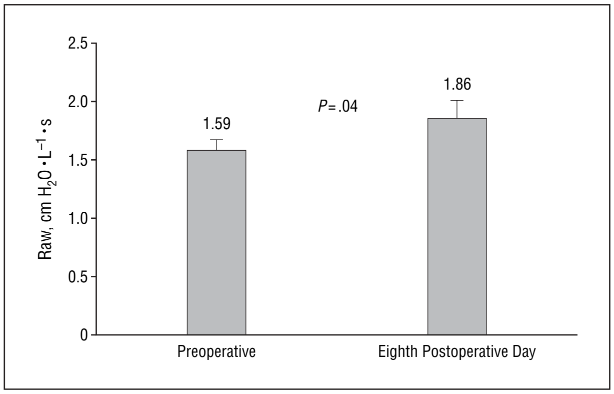

Figure 3. Mean preoperative and eighth postoperative day airway resistance (Raw) values in the laparoscopic cholecystectomy group. Error bars represent SEM.

nificant increase in BF (LC group: $P=.01$; 95% CI, 20.14-25.02; OC group: $P=.05$; 95% CI, 20.67-30.21) and the $P_{0.1}$ (LC group: $P=.001$; 95% CI, 1.78-2.39; OC group: $P=.01$; 95% CI, 1.65-2.17) for both surgical methods.

In contrast to the OC group, LC patients displayed an early (second postoperative day) significant increase in $Z_{m,insp}$ ($P<.001$; 95% CI, 3.9-5.34). This variable remained increased until the eighth day after LC and was accompanied by a small reduction in mean V_T/T_i, although the statistical significance of these changes was not established.

The T_i/T_{TOT} displayed a significant decrease ($P=.01$; 95% CI, 0.36-0.40) on the eighth postoperative day only for the LC patients (**Figure 2**).

Postoperative Raw values showed a significant increase ($P=.04$; 95% CI, 1.54-2.18) only in the LC group (**Figure 3**).

Differences across time between the 2 groups showed a significant difference in T_i/T_{TOT} ($P=.02$) and BF ($P=.08$) 2 days after surgery.

COMMENT

The possible effects of postoperative analgesia on the values of indexes measured in this study have to be definitely excluded. Absorption after intramuscular injection of meperidine hydrochloride has a plasma elimination half-life of approximately 3 to 6 hours in healthy individuals.[18,19] Proper absorption of this drug is better ensured by injection in the deltoid rather than the gluteus muscle,[20] as was our practice.

With respect to the control of breathing in the postoperative period for cholecystectomy, previous studies examining T_i[2,3] and BF[1-3] on the first[2,3] and third[2] postoperative days after laparoscopic[3] and open[2] surgical procedures and 3 hours[1] after the former are in agreement with our findings on the second postoperative day for both surgical methods. The decrease in T_i found 48 hours after surgery for all analyzed patients may be explained by the corresponding increase in BF. In addition, persistence of the elevated BF in both groups is probably related to restrictive effects, which compromise respiratory system compliance. For the LC patients, these effects are attributed to augmented intra-abdominal pressure as a result of the introduction of pneumoperitoneum by CO_2 insufflation, which affects respiratory mechanics.[21,22] Restrictive effects for patients who underwent OC have been thought to be due to either diaphragmatic dysfunction induced by upper abdominal surgery[9,10,21] or abdominal wall trauma, as is evident from the shift from predominantly abdominal to rib cage breathing movement after OC.[9,23]

Changes in pulmonary afferent activity once inspiration has begun are reflected in the slope of integrated phrenic nerve activity, the mechanical transformation of which is the mean V_T/T_i.[24] For this particular variable, which was examined 24 hours[2] and 72 hours[2] after OC and 3 hours[1] and 24 hours[3] after LC, statistically significant differences compared with preoperative values were only detected in 1 study[2] 72 hours after OC during room air breathing in the supine position. In the present study, significant differences in V_T/T_i were not found on either the second or eighth postoperative day for both groups. The relative stability of V_T/T_i may be attributed to the small unidirectional change in both variables of the ratio.

The T_i/T_{TOT}, which indicates the relationship between inspiration and expiration, providing a crude measure of the degree of airway obstruction,[25] had previously been examined 3 hours[1] and 24 hours[3] after LC. Its values were found to be significantly decreased 3 hours after LC[1] compared with those before surgery, whereas in this study, a significant reduction in T_i/T_{TOT} was detected on the eighth day after LC. The following findings are indicative of a restrictive process operating under laparoscopic surgical conditions: (1) the statistically significant lower T_i/T_{TOT} for the LC group compared with the OC group on the second postoperative day, accompanied by a lower value in the former group 8 days after surgery (although without a significant difference between the groups at this time), and (2) the statistically significant difference between preoperative and eighth postoperative day measurements in the LC group. This seems to be in accordance with the findings of previous researchers.[21,22]

Furthermore, in the present study, changes in $P_{0.1}$ found on the second postoperative day are in agreement with those of a previous study[1] in which a trend for elevation in $P_{0.1}$ was demonstrated 3 hours after LC. The increase in $P_{0.1}$ observed in both groups 48 hours after surgery can possibly be attributed to some type of diaphragmatic impairment caused by generation of the phrenic nerve inhibitory reflex[10,26-30] during surgery. This effect is due to either sympathetic or parasympathetic stimulation arising from manipulations (including the use of trocars) of intra-abdominal visceral organs with corresponding nerves adjacent to reflexogenic splanchnic areas.[1] Particularly for LC, the phrenic nerve inhibitory reflex results in reduced neural impulse to the diaphragm,[1,11] the recovery of which seems to start by the first postoperative day.[11]

The $Z_{m,insp}$ ($P_{0.1}/[V_T/T_i]$)[5,6] is classically defined as the sum of forces that must be overcome during inspiration. These forces include resistance, lung elastance, and inertance as well as chest wall deformation.[6] The statistically significant increase in $Z_{m,insp}$ on the second day after LC observed in this study could be explained by progressive alterations in lung and chest wall mechanics due to CO_2 insufflation.[31] Data for $Z_{m,insp}$ 2 days after LC, in association with the significantly lower T_i/T_{TOT} values registered at this time for LC vs OC patients, are indicative of a higher degree of airway obstruction for those undergoing LC. This suggests a prolonged expiratory time for the LC group. This fact is supported by our findings for BF, where mean percentage changes from baseline to the second postoperative day were higher for patients undergoing OC.

The Raw 2 days after LC and OC has not been found to be significantly changed by previous researchers,[4] whereas in our study, this variable was shown to be significantly increased only in LC patients by the eighth postoperative day. This increase in the LC group seems to parallel the concomitant decrease in T_i/T_{TOT} and the increase in $Z_{m,insp}$.

A global consideration of the previous findings is suggestive of a more prominent and prolonged effect of LC on specific aspects of control of breathing and respiratory mechanics, compatible with some kind of diaphragmatic dysfunction and a degree of airway obstruction, respectively.

In support of diaphragmatic dysfunction after LC, a variety of studies[1,32,33] have attributed this effect to the abdominal insufflation causing (1) limitation in diaphragmatic excursion and "stiffening" of the diaphragmatic abdominal part of the chest wall[32]; (2) interactions among the rib cage, abdomen, and diaphragm resulting from abdominal distention[33]; and (3) reflexic inhibition of phrenic nerve output,[1] whereas postoperative residual pneumoperitoneum, per se, which resolved during the first week after surgery,[34] did not explain the diaphragmatic dysfunction after LC.[35] Regarding OC, Dureuil et al[28] showed that abdominal wall trauma may have nothing to do with diaphragmatic weakening.

Furthermore, gas insufflation in the abdomen might also be responsible for the increase in Raw found in this study. A smaller airway caliber is known to be associated with the reduction in lung volume resulting from decreased lung compliance, which is an established observation with respect to the laparoscopic procedure.[31] This reduction in lung volume has been thought to be associated with surfactant dysfunction[36] and nonuniform lung distortion caused by the pressure generated in the abdomen during insufflation.[36]

In the present study, the longer-term effects of LC on the respiratory pattern and mechanics, which do not seem to reflect primary effects on $P_{0.1}$, provide indirect evidence of the emergence of a degree of diaphragmatic dysfunction after application of this surgical method. The observed changes might be attributed to the mechanical derangement induced by the introduction of pneumoperitoneum despite that the gas is readily released from the abdominal cavity after the operation.

Previous studies[37-39] have assessed the effects of abdominal insufflation on cardiopulmonary function and physiologic variables of the respiratory system shortly after LC. These studies claimed that intra-abdominal pressure created by abdominal gas insufflation is associated with a depressed cardiac index,[38,39] decreased lung compliance,[37,38] and respiratory acidosis.[37] It has also been suggested that changes in cardiopulmonary function after upper abdominal laparoscopic procedures warrant cautious invasive monitoring and careful interpretation in American Society of Anesthesiologists' class III and IV patients.[38] Other researchers are in support of the application of gasless laparoscopy in high-risk patients[39] to avoid the aforementioned cardiopulmonary complications.

Our findings concerning changes in the control of breathing (lower T_i/T_{TOT}) and lung mechanics (higher Raw) associated with LC were shown to be present later in the postoperative period (eighth postoperative day) than other functional alterations detected in previous studies.[1-4,7] This implies that some of the changes induced by the laparoscopic technique may be more sustained than previously thought. Also, the magnitude of detected changes in this study is small, and their clinical significance should be further discussed. Increased Raw imposes an additional load in the total work of breathing,[40] which must be overcome by a presumably weakened dysfunctional diaphragm. This creates a kind of imbalance between load and respiratory pump capacity (respiratory muscles).[41] Under normal conditions, the reserves of the respiratory system are more than sufficient to cope with this disequilibrium. Theoretically, this will probably not be the case for a respiratory system with impaired functional reserves.

Given that, according to a variety of studies, the initial event that causes the respiratory alterations after laparoscopic procedures[37-39] is the magnitude of the created intra-abdominal pressure by gas insufflation, some researchers have supported that operating under reduced pressures[42] or indirectly achieving lower pressures by using the abdominal wall lift method[22] seems to have a beneficial effect on classic laparoscopy-induced respiratory changes.

In conclusion, although the laparoscopic technique is considered to be the preferred method for gallbladder removal owing to its minimal invasiveness, it seems to be involved in a small but sustained diaphragmatic dysfunction and airway obstruction. Although the exact clinical impact of this particular observation cannot be clearly defined, it is logical to expect an unfavorable effect of the laparoscopic technique in patients with compromised lung function. Alternative surgical measures, such as operating under reduced intra-abdominal pressure or use of the abdominal wall lift method, should be considered in this context.

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